HEALTH AND NUTRITION NEWS

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Prefatory Note

Our future expectations for the NIHN, with respect to public health nutrition activities

Kayoko Sato
Chief of Public Health Nutrition,
Department of Health Promotion and Research,
National Institute of Public Health

The reform of the medical care system aims to shift the current system into a structure more stressing disease prevention. It is a big reform in the health, medical and welfare sectors, where the target issues extend across health promotion, treatment and home care. In order to control lifestyle-related diseases, the measures involving the concept of metabolic syndrome are enhanced. The national health insurance associations will be obligated to provide the health check/guidance, by which effectiveness of health guidance can be well secured. Besides, it is important to ensure harmonization of three schemes; health promotion, medical and nursing care insurance.

A control program of lifestyle-related diseases starts from 2008, focusing on prevention of lifestyle-related diseases (obesity, diabetes, hypertension, hyperlipidemia etc.) derived from metabolic syndrome, cardiovascular diseases (ischemic heart disease, cerebral stroke) and diabetes complications, through the lifestyle modification on unbalanced diet, lack of exercise, stress, alcohol drinking, smoking etc. This program combines high-risk approach and population one, considering prevention of impaired vital functions and being in need of nursing care. The health services will greatly change, and the public health nurses and the registered dietitians are expected to take more important roles to implement the new health services. The National Institute of Public Health (NIPH), therefore, starts the human resource development program in the field of health services from 2007.

NIPH provides various courses; long-term training courses to develop the highly-specialized professionals in the field of health, medicine and environmental health in local public authorities (Doctor of Public Health Course, Master of Public Health Course, Diploma in Public Health Course: 3 months - 3 years), short-term special course for continuing education in public health (about one month), pinpoint seminars for the latest and urgent public health issues (a few days), and distant learning course using the Internet. For which, we receive supports from the experts in the National Institute of Health and Nutrition (NIHN).

Talking about “dietitian”, I heard that Dr. Tadasu Saiki (the founding Director-General of NIHN), who established the base of nutritional sciences and started the training of dietitians in 1920, stated that “Dietitians should voluntarily advocate the importance of nutrition and appropriate diet to as many people as possible, instead of waiting for their visits”. The Japanese term of “dietitian” therefore contains the meaning of “serve” (instead of “teach”, which is typically included in the health-related qualifications). Following promulgation of the Public Health Center Law, the public health centers were established across the country, where the dietitians were also assigned. This was the origin of “public health dietitian”, who worked actively on the educational activities in the field of public health nutrition including the “Kitchen car” program to overcome the malnutrition period. The NIPH was founded in 1938, though it was merged with the NIHN in 1940 to become the “Research Institute of Health Sciences (RIHS)”, where Department of National Nutrition and Department of Dietitian Training were established. Later, following separation of the NIPH from the RIHS in 1947, Department of Nutrition was established in the NIPH, where the training of dietitian has been continued. The name of this training course changed in line with social situations, and it is presently named as “Pubic Health Nutrition Course”. The NIHN evolved as a specialized nutrition research institute, and contributed to nutritional improvement and public health activities; e.g. establishment of Recommended Dietary Allowances (present “Dietary Reference Intakes), National Nutrition Survey (present “National Health and Nutrition Survey”). In this way, the NIHN has been taking the unique approaches that are different from the NIPH.

Recently, it has been reported that one in two Japanese males aged 40-74 years were at risk of metabolic syndrome (Report of the National Health and Nutrition Survey, 2004). This problem concerns not only themselves, but also their children. Another survey reported that 10% of under-four children do not take breakfast everyday, which was likely to be associated with their mothers’ dietary habits (Children and Infant Growth Survey, 2005). Similarly, our survey on the infants aged 18 months also revealed that the proportions of infants and their mothers who did not take breakfast everyday were 20% and 40%, respectively. No matter whatever the reason is, skipping meals of infants are of responsibility of their parents. While raising motivation and temporal behavioral changes may be possible in adults, it is not easy to start and continue a new lifestyle. It is therefore obvious that food education from an early age should be important and promising. For which, health guidance and “Shokuiku” targeting children (with their family) could be effective and thus, we place our hopes on implementation of the “Basic Plan for Promotion of Shokuiku”.

The NIHN made the organizational reformation in 2006, with the second mid-term goal of “The NIHN to be open to the public”. We can see enthusiasm for achieving its goal in the staffs and concerned persons. Field activities based on the scientific evidences are now required, and thus, we expect that the NIHN will keep working on the researches and providing information to support the registered dietitians, dietitians and other nutrition-related specialists.

** The original Japanese version was translated by Project for International Research and Development, NIHN*

Food Function and Labeling Program

Junichi Nagata
Food Function and Labeling Program

Food Function and Labeling Program is composed of three projects; Project for Food Component Analysis, Project for Complementary Factors, and Project for Food Functionality. Here, I would like to introduce the outlines of researches at each project, together with the latest research issues on lipid as a functional component.

Project for Food Component Analysis is in charge of technical aspects of the food and health administration, which is implemented by the Ministry of Health, Labour and Welfare. In particular, this project undertakes the analytical tests of the foods labeled as "Food for Special Dietary Uses", and of those with nutritional labeling, using the food samples collected by the Ministry of Health, Labour and Welfare, in order to assess if the nutrients and food components are labeled correctly. We also examine the submitted application forms for “Food for Specified Health Use”, and work on the proper labeling on foods. Furthermore, in order to respond technically to new food components of "Food for Specified Health Uses", the standardization is made for the analytical technique and the standard goods of these food components. A great effort is made to improve the environment for correct and effective implementation of the above food analyses.

Project for Complementary Factors works to explore the complementary factors that have positive effects on prevention and treatment of chronic diseases (e.g. lifestyle-related diseases). These complementary factors are screened from the food-derived components that possibly have physiological functions, and their effectiveness is scientifically evaluated by cell or animal models. In this way, this project investigates the possibilities of developing a new method to prevent and treat chronic diseases, using the complementary factors.

Project for Food Functionality aims to develop tailor-made functional foods, focusing on the functional food components with inhibitory effects against atherosclerosis. The functional food components mainly studied are docosahexaenoic acid (DHA) (n-3 fatty acid), Sesamin derived from sesame seeds, antioxidants etc. In order to develop antiatherosclerotic functional foods, this project undertakes screening for the food components, by investigating the effects on atherosclerosis risk factors, inflammation and the inhibitory factors of endothelial cell injury.

In addition to these administrative affairs related to food component analyses of “Food for Special Dietary Use” and labeling, our program collects the information on the foods taken for the sake of fitness, and attempts the advanced uses of functional components, through the basic researches on the functionality of food components and health effects.

As a member of Project for Food Component Analysis, my main duties are the analyses of “Food for Special Dietary Uses” and “Food for Specified Health Uses”, and the technical supports for the food and health administration. In addition, I have been working on the examination of the functionality of lipid and nutritive composition of foods.

Despite that lipid is an essential nutrient for living body working as energy source, component of cell membrane, prohormone and carrier of lipid-soluble component, this is the typical nutrient that has a negative image as a food component worsening lifestyle-related diseases. Yet, the past studies have explored the lipid-soluble components with various physiological functions, and thus some of them are utilized as functional food materials; phytosterol, fish oil (EPA, DHA), middle-chain fatty acids, structured lipid and conjugated linoleic acid (CLA).

Since excess lipid intake would increase the risk of developing lifestyle-related diseases, lipid is regarded as the food component that we should be cautious about its quality and quantity taken. Besides, it is reported that excess intake of fat/oil widely used for cooking/processing foods (e.g. the one with high proportion of trans fatty acids) is associated with the increased risk of developing lifestyle-related diseases. Under this circumstance, more attention has been paid to the researches on food materials, where fat/oil with less absorption into the body, low calorie fat/oil and alternative fat/oil are developed. While there remain many problems with its application in cooking and taste, it is expected that this type of fat/oil with various functionality will be widely used. Now, I am trying to develop edible fat/oil effective to prevent lifestyle-related diseases, through evaluation of new functional fat/oil for its design, physiological functions, nutrition and safety.

A thought on health and nutrition research at a pet shop?

Takashi Kumae
Health Promotion and Exercise Program

Do you know that the number of pet dogs is growing beyond the number of children? In 2005, the number of new born babies in Japan was 1.06 million, and the number of registered pet dogs was 6.26 million (2003). A survey conducted by the pet food industry association in 2005 estimated the number of pet dogs to be 130.6 million. When I go to work or take a walk, I often see people with their dogs. Most supermarkets have the pet section, where dog foods etc. are available. The pet-related market has about one trillion yen business in 2005. In my childhood, it was common to give the leftovers to dogs and we rarely bought any special foods for dogs. At that time, the average lifetime of dogs was shorter than now, for about four or five years. Nowadays, special food for older dogs is also available. The average lifetime of dog is now 12-14 years, though it varies by its kind to some degree. Seeing-eye dogs even work up to 10 years old. Whilst there is no statistical data, it is obvious that their lifetime has been increasing dramatically. One of the reasons seems to be the widespread use of dog food. Looking at the prolonged lifetime by change of diet, we can say that dogs have shown the importance of nutrition on their health.

I started this article with a topic on pet dogs. Why? Well, let me move to the topic of nutrition for human now. It was not until I came to this institute that I joined in human metabolic studies. I am grateful to Dr. Nishimuta (Project for Bio-index, Nutritional Epidemiology Program) for giving me an opportunity to participate in a 21 day study on nonspecific immune function. I dare not to mention its results here, as the published article of this study is now available on the web. Since I had never been involved in this type of human study, everything was new and surprising to me. I was impressed with the cooperative attitudes of 11 female college students as the participants. In this study, both food intake and excretion were checked. Collecting the excretory substances should be quite tough, though it was found that measuring food intake was even more laborious. I was impressed with the study team who cooked, served and measured those foods, and also with the study participants who had to eat up all the provided food, while the same menu was served every four days. I saw the contents of *miso* soup by chance, where *tofu* was cut into so tiny dice size. This effort was to make sure that all the participants take the same amount of foods and ingredients. If I were the study participant, I would run away on the fifth day.

Since dogs are given same food once or twice a day regularly, experiments on dogs could be easy. One dog food promo says “In order to build the anti-aging and strong body, this dog food is supplemented with anti-oxidant bio-factor and the nutrients that are likely to decrease with age”. We, human, also might need such food in this aging society, though it must be practically difficult to undertake the experimental studies on the elderly. Even if we develop well-balanced dried food like dog food, it is not feasible to recommend people to take it all the time to have healthier and longer lives, as it would decrease one’s quality of life (QOL). Now, let’s think how can the health and nutrition researches intervene for capricious humans who have various demands?

Exercise Guideline for Health Promotion 2006

Let's target 23 Ex (METs・hour) per week by physical activity, of which 4 Ex by active exercise!

Izumi Tabata
Health Promotion and Exercise Program

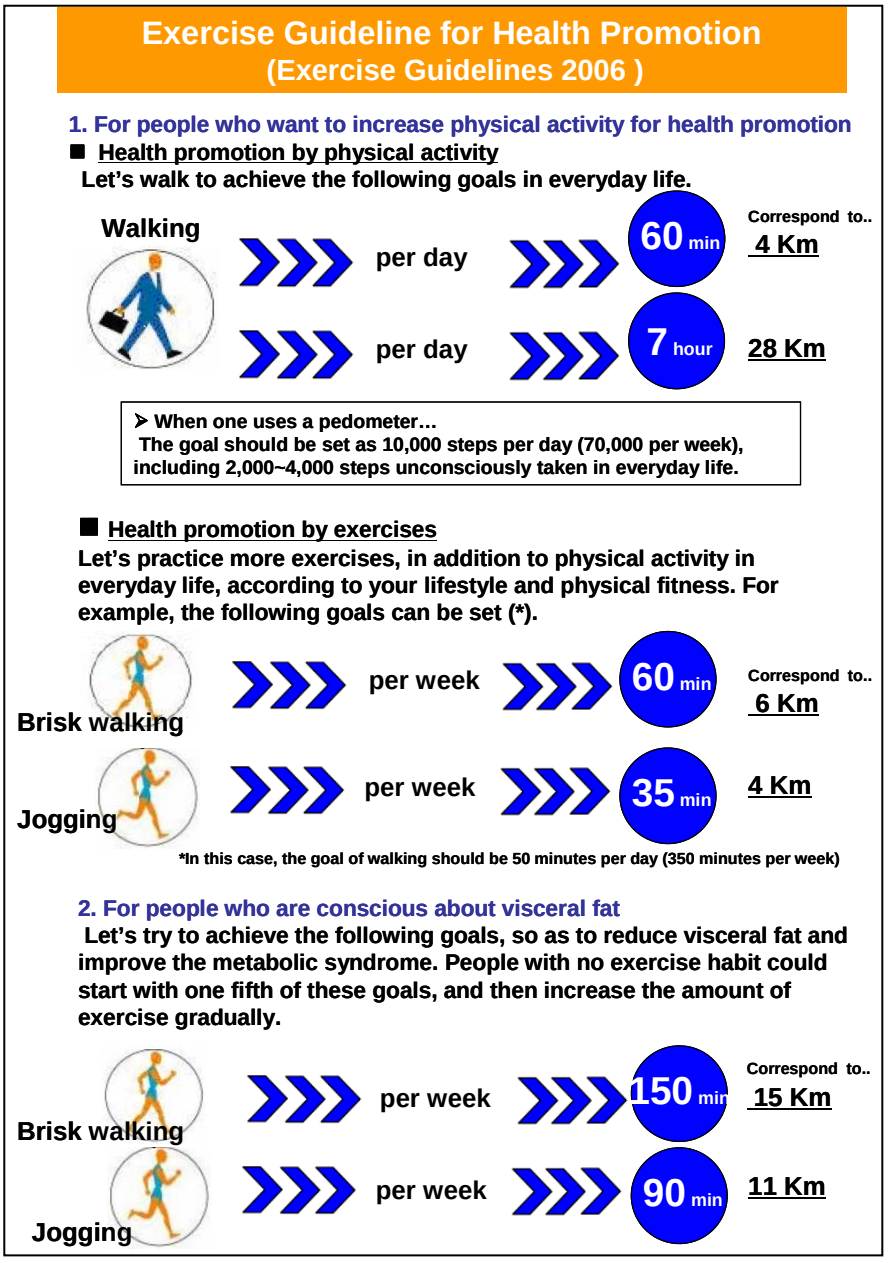
Following establishment of "Exercise and Physical Activity Reference Quantity for Health Promotion (EPARQ2006): Physical Activity, Exercise and Physical Fitness" (as introduced in Health and Nutrition News No. 15) that determined the references of physical activity, exercise and physical fitness, and reported the scientific evidences, the Ministry of Health, Labour and Welfare issued the "Exercise Guidelines for Health Promotion 2006 (Exercise Guidelines 2006)". While EPARQ2006 was prepared for the experts on exercise, the Exercise Guidelines 2006 was developed to encourage the nation to increase the amounts of physical activity and exercise for health promotion.

Under the slogan written on the top of this page (with title), the Exercise Guidelines 2006 were established for the nation to understand the EPARQ2006 very well. In addition, the Exercise Guidelines 2006 introduces how to relieve metabolic syndrome, which was not included in the EPARQ2006.

The unit for the quantity of physical activity and exercise was set as "exercise (Ex)". For physical activity, 1 Ex corresponds to walking/child care/car washing/house cleaning for 20 minutes, brisk walking/bicycling/ show shovel for 15 minutes, and carrying heavy loads for 7 minutes. As for exercise, 1 Ex corresponds to bowling/volley ball for 20 minutes, water exercise/jazz dance/badminton for 15 minutes, and aerobics/jogging for 9 minutes.

If we practice on average 3 Ex per day by incorporating these activities actively in everyday life, we can meet the references in the EPARQ2006. By which, it is expected that lifestyle-related diseases (e.g. diabetes) can be prevented.

Likewise, regular exercise can reduce waist circumference, eventually relieving metabolic syndrome.



Latest Research

Effects of simultaneous intakes of indigestible dextrin and diacylglycerol on lipid profiles in rats fed cholesterol diets.

Jun-ichi Nagata (Food Function and Labeling Program)

Now, in Japan, there are many types of health foods that claim physiologic benefits in the market. Although the functionalities are scientifically proven for some foods (food with health claims), there are also “so-called” health foods which do not necessarily have adequate scientific support. Regardless of the proof of scientific evidences, there is a strong trend that these health foods are taken simply based on the images from their promo words. It is therefore possible that some of the consumers may take health foods inappropriately (e.g. those who take too much health food with expectation of physiologic functions, those who take various health foods with similar effects simultaneously). Whilst the past food science studies have investigated the effectiveness of each particular health food or food component in details, little has been studied on the physiologic effects and safety of simultaneous intake of several functional foods so far yet.

Under this circumstance, we investigated whether simultaneous intake of health foods or food constituents, which are scientifically claimed to decrease risk factors for lifestyle-related diseases (such as obesity and hyperlipidemia), produce any physiological advantage with respect to lipid profiles and body fat accumulation. In the present study, we focused on the effects of a combination of diacylglycerol (DG) which is recognized to possess physiologic effects, such as prevention of obesity and reduction of serum lipid levels and indigestible dextrin (IDex) which modulates intestinal functions and also possibly decreases serum lipid level. For which, five-week-old male Wistar rats were fed a cholesterol-containing diet with DG and IDex for 28 days.

IDex significantly decreased serum triacylglycerol concentration and increased the length of small intestinal villi, which indicates that IDex acts as a dietary fiber. On the other hand, DG produced significant decrease in serum high-density lipoprotein (HDL) cholesterol concentration and significant increases in liver cholesterol and triacylglycerol concentration. The physiological effects of DG, however, were not clearly detected under the present experimental conditions.

In conclusion, IDex intake characteristically decreased serum triacylglycerol concentrations in rats fed a cholesterol-containing diet, no additive or synergistic interactions were observed during feeding with the combined DG and IDex diet. These results indicate that simultaneous intake of food components with similar physiologic functions does not necessarily produce additive or synergistic physiologic benefits.

In order to utilize widely available functional foods appropriately and safely for prevention/improvement of lifestyle-related diseases, further studies will be needed to examine various dietary conditions and the combinations of functional foods with different physiologic functions.

Effects of simultaneous intakes of indigestible dextrin and diacylglycerol on lipid profiles in rats fed cholesterol diets.

Nutrition. 2006; 22: 395-400.

Nagata J, Saito M

Division of Food Science, National Institute of Health and Nutrition, Tokyo, Japan

Abstract: **OBJECTIVE:** Indigestible dextrin (IDex) and diacylglycerol (DG) are food components with physiologic effects on lipid metabolism. Because simultaneous intake of dietary components with similar physiologic functions may produce a beneficial decrease in risk factors for lifestyle-related diseases, we investigated the physiologic effects of simultaneous IDex and DG intake. **METHODS:** Five-week-old male Wistar rats were fed a cholesterol-containing diet with IDex and DG (separately and combined) for 28 d. **RESULTS:** IDex significantly decreased serum triacylglycerol concentration and increased the length of small intestinal villi, whereas DG produced significant decreases in serum high-density lipoprotein cholesterol concentration and significant increases in liver cholesterol and triacylglycerol concentrations. **CONCLUSIONS:** IDex intake characteristically decreased serum triacylglycerol concentrations, although no additive or synergistic interaction between DG and IDex was observed. These results indicate that simultaneous intake of food components with similar physiologic functions do not necessarily produce additive or synergistic physiologic benefits.

Latest Research

Dietary glycemic index and metabolic risk factors: a cross sectional study of Japanese female farmers.

Kentaro Murakami, Yoshiko Takahashi, Satoshi Sasaki (Nutritional Epidemiology Program)

Dietary carbohydrate raises blood glucose, but the blood glucose response varies substantially among different carbohydrate-containing foods. This varied glycemic response is quantified according to the glycemic index (GI). The GI of a food is defined as the 2-h incremental area under the blood glucose response curve after consumption of a food portion containing 50 g of available carbohydrate, divided by the corresponding area after consumption of 50 g glucose, and multiplied by 100 to be expressed as a percentage (GI of glucose = 100). Glycemic load (GL) is calculated by GI multiplied by available carbohydrate content.

Recent results from observational studies have suggested that diets with a low GI, a low GL, or both have a beneficial effect on several metabolic risk factors. However, almost all studies of dietary GI or GL and metabolic risk factors have been conducted in Western countries, whereas, to our knowledge, only one small study was carried out in Asian countries, including Japan. For Japanese people, rice is the food that contributes most to total carbohydrate, which is a characteristic seldom observed in Western people. Therefore, a different association of dietary GI or GL and metabolic risk factors may exist between Western and Japanese populations. Consequently, we examined the cross-sectional associations between dietary GI and GL and several metabolic risk factors in a group of apparently healthy Japanese women with traditional dietary habits.

The subjects were 1345 Japanese female farmers aged 20-78 y from 5 regions of Japan. Dietary habits during the past one month were assessed with a self-administered diet-history questionnaire (DHQ), from which dietary GI and GL were calculated. Height and weight were measured and fasting blood samples were collected.

White rice was the major contributor to dietary GI and GL (59%) in the present study, whereas in Western populations, dietary GI and GL are determined by a variety of food including potatoes, breakfast cereals, bread, and rice (4-8%). **Figure 1** shows the associations between dietary GI and metabolic risk factors. Dietary GI was positively associated with body mass index, fasting serum triacylglycerol, fasting plasma glucose and Hb A_{1c}. **Figure 2** shows the associations between dietary GL and metabolic risk factors. Dietary GL was positively associated with fasting serum triacylglycerol and fasting plasma glucose and negatively associated with serum HDL cholesterol.

Although the major contributor to dietary GI and GL of Japanese women is very different from that of Western populations, the results showed that dietary GI and GL were associated with several metabolic risk factors. Whilst the increase of metabolic syndrome and Type 2 diabetes might be associated with dietary GI and GL (or white rice), further studies are needed to examine the associations in details.

(This study was undertaken as a joint research with Professor Fujio Kayama in the Division of Environmental Medicine, Center for Community Medicine, Jichi Medical University)

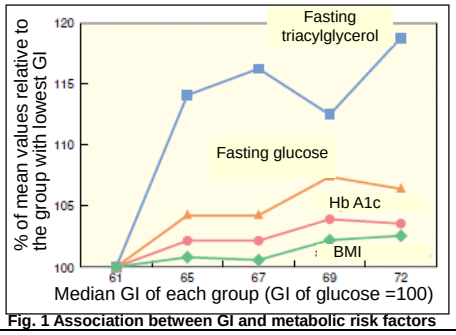


Fig. 1 Association between GI and metabolic risk factors

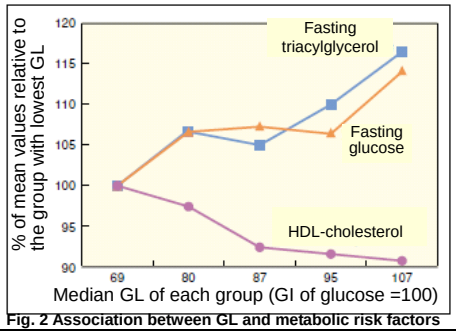


Fig. 2 Association between GL and metabolic risk factors

Dietary glycemic index and load in relation to metabolic risk factors in Japanese female farmers with traditional dietary habits.

American Journal of Clinical Nutrition. 2006 May;83(5):1161-9

Murakami K [1)], Sasaki S [1)], Takahashi Y [1)], Okubo H [2)], Hosoi Y [1)], Horiguchi H [4)], Oguma E [3,4)] and Kayama F [3,4)]

1) National Institute of Health and Nutrition, Tokyo, Japan
2) Department of Nutrition Sciences, Kagawa Nutrition University, Saitama, Japan
3) Division of Environmental Medicine, Center for Community Medicine, Jichi Medical University, Tochigi, Japan
4) Core Research for Evolutional Science and Technology, Japan Science and Technology Cooperation, Kawaguchi City, Japan

Abstract: **BACKGROUND:** Little is known about the relation of dietary glycemic index (GI) and glycemic load (GL) to metabolic risk factors, particularly in non-Western populations. **OBJECTIVE:** We examined the cross-sectional associations between dietary GI and GL and several metabolic risk factors in healthy Japanese women with traditional dietary habits. **DESIGN:** The subjects were 1354 Japanese female farmers aged 20-78 y from 5 regions of Japan. Dietary GI and GL were assessed with a self-administered diet-history questionnaire. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Fasting blood samples were collected for biochemical measurements. **RESULTS:** The mean dietary GI was 67, and the mean dietary GL (/1000 kcal) was 88 (GI for glucose = 100). White rice (GI = 77) was the major contributor to dietary GI and GL (58.5%). After adjustment for potential dietary and nondietary confounding factors, dietary GI was positively correlated with BMI (n = 1354; P for trend = 0.017), fasting triacylglycerol (n = 1349; P for trend = 0.001), fasting glucose (n = 764; P for trend = 0.022), and glycated hemoglobin (n = 845; P for trend = 0.038). Dietary GL was independently negatively correlated with HDL cholesterol (n = 1354; P for trend = 0.004) and positively correlated with fasting triacylglycerol (P for trend = 0.047) and fasting glucose (P for trend = 0.012). **CONCLUSIONS:** Both dietary GI and GL are independently correlated with several metabolic risk factors in subjects whose dietary GI and GL were primarily determined on the basis of the GI of white rice.

Latest Research

Garcinia cambogia, as a dietary supplement for suppressing fat accumulation: Attention to its toxicity in testis!

Morio Saito (Food Function and Labeling Program)

Garcinia cambogia, a kind of herb, is an evergreen tree native to India and Southeast Asia, which bears orange-size fruits between May and September. The fruit or rind has a strong acid taste. Ripen ones can be eaten raw, and the dried fruit/rind has been used for centuries for flavoring curry or preservation of salted fish. The rind contains (–)-Hydroxycitric acid (HCA), which is popularly used as an ingredient of dietary supplements for weight loss.

HCA is a competitive inhibitor of ATP citrate lyase with citric acid. This inhibitory action of HCA reduces the acetyl-CoA pool, resulting in the suppression of fat synthesis from glucose and body fat accumulation.

HCA has been shown to be active in reducing body weight and suppressing body fat accumulation in experimental animals. Similarly, several human studies reported that HCA suppressed the body fat accumulation, though there are many studies that rejected its effect. Therefore, no consensus has been made yet on the effectiveness of HCA in humans due to various influencing factors (e.g. characteristics of study subjects, dietary patterns, amount of HCA intake).

As for the safety of *Garcinia*, it has been considered safe, due to the long dietary history in Southeast Asia and also based on the result of an acute toxicity test using rats (LD50 5,000mg/kg BW or higher). In our study [1)], however, when Zuker obese rats were fed diets containing HCA, high dose of *Gercinia* (154 mmol HCA/kg diet) showed significant suppression of epididymal fat accumulation, but 102 mmol/kg diet or higher (778 mg HCA/kg BW/day) caused testicular toxicity (testicular atrophy and impairment of spermatogenesis). Another study also observed similar findings, and the Ministry of Health, Labour and Welfare of Japan officially reported the testicular toxicity of *Garcinia*. It has also been presumed that the testicular toxicity could be caused by HCA itself.

For commercially available dietary supplements containing *Garcinia cambogia* in Japan, the recommended intake range is 750-1500mg of HCA/d per person. For example, the recommended intake range for a subject with body weight 50kg is 15-30 mg HCA/kg Bw/d, which is one-twentysixth to one-thirteenth of no observed adverse effect level (NOAEL)(The NOAEL of 51mmol HCA/kg diet corresponds to 389 mg HCA/kg Bw/d). Therefore, safety for human consumption is not essentially ruled out. However, a variety of *Garcinia cambogia*-containing so-called health foods are sold on the market, and the tablet- and capsule-type dietary supplements are easily taken in excess. Besides, the sensitivity to HCA may vary considerably from person to person. Moreover, acetyl-CoA production from glucose in humans has been reported to be approximately one-fortieth of that in rats because of low activity of ATP-citrate lyase in humans. It is therefore unlikely that obese people would experience a suppression of body fat accumulation by HCA except in the setting of an unphysiological high-carbohydrate and low-fat diet containing very high level of HCA.

This is the first published report of the testicular toxicity of HCA-containing *Garcinia cambogia*, and we do not currently know which constituent is responsible for the toxicity. Its intake therefore should be restricted, until its safety can be confirmed. We also investigated the mechanism of the testicular toxicity of *Garcinia*[2)], and its effect on female rats[3)], and no deleterious influence was observed in the female rats. And we hypothesized from our results[2)] that HCA-mediated inhibition of ATP citrate lyase in rats fed GA leads to diminished accumulation of MAS substances, thus resulting in impairment of spermatogenesis. This study was conducted as one of the prioritized researches titled “Evaluation of physiological effectiveness and health effects of foods and food components” during the period of the First Mid-term Plan (2001-2006).

<Reference>

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High dose of *Garcinia cambogia* is effective in suppressing fat accumulation in developing male Zucker obese rats, but highly toxic to the testis.

Food and Chemical Toxicology. 2005; 43: 411-419

Saito M[1)], Ueno M[1)], Ogino S[1)], Kubo K[1)], Nagata J[1)] and Takeuchi M[2)]

1. Division of Food Sciences, National Institute of Health and Nutrition, Tokyo, Japan
2. Sapporo General Pathology Laboratory Co., Ltd., Hokkaido, Japan

Abstract: We investigated the ability of *Garcinia cambogia* extract containing (-)-hydroxycitric acid (HCA) to suppress body fat accumulation in developing male Zucker obese (fa/fa) rats. We also examined histopathologically the safety of its high doses. Diets containing different levels of HCA (0, 10, 51, 102 and 154 mmol/kg diet) were fed to 6-week-old rats for 92 or 93 days. Each diet group was pair-fed to the 154 mmol HCA/kg diet group. Epididymal fat accumulation and histopathological changes in tissues were observed. The highest dose of HCA-containing Garcinia cambogia (154 mmol HCA/kg diet) showed significant suppression of epididymal fat accumulation in developing male Zucker obese rats, compared with the other groups. However, the diets containing 102 mmol HCA/kg diet and higher (778 and 1244 mg HCA/kg BW/d, respectively) caused potent testicular atrophy and toxicity, whereas diets containing 51 mmol HCA/kg diet (389 mg HCA/kg BW/d) or less did not. Accordingly, 51 mmol HCA/kg diet (389 mg HCA/kg BW/d) was deemed to be the no observed adverse effect level (NOAEL).