Review Article

Functional lipids and the prevention of the metabolic syndrome

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The metabolic syndrome is increasingly prevalent in worldwide. The quality and quantity of dietary lipids could be important modulators associated with the cardiovascular morbidity and mortality. At present, functional lipids such as conjugated linoleic acid (CLA) and phospholipids have attracted considerable attention because of their beneficial biological effects in attenuating metabolic syndrome. Supplementation of CLA reduces abdominal white adipose tissues, serum triacylglycerol (TAG) level, and liver TAG level in obese Otsuka Long-Evans Tokushima Fatty OLETF rats. These effects were attributed to enhanced fatty acid beta-oxidation and suppressed fatty acid synthesis in the liver. In addition, CLA enhanced energy expenditure in these rats. Anti-hypertensive properties of CLA have also been demonstrated. In obese/diabetic OLETF and Zucker rats, feeding of CLA prevented the development of obesity-induced hypertension. This was associated with an altered production of physiologically active adipocytokines, such as adiponectin, leptin and angiotensinogen. In addition, CLA could alleviate the development of insulin resistance and fatty liver. Dietary phospholipids have physiological functions that are different to dietary TAG. We recently reported that phosphatidylcholine (PC) alleviated orotic acid-induced fatty-liver through the suppression of hepatic lipogenesis in rats, and omega3-PC from salmon roe prevented the development of obesity-related diseases through the suppression of lipogenic gene expressions and the enhancement of lypolytic gene expressions in the liver of obese rats. However, reports which studying the nutritional functions of minor phospholipids, such as phosphatidylinositol (PI), are scarce. Our study indicated that dietary PI lowered lipids in the plasma and liver by suppressing hepatic TAG synthesis.

Key Words: lipids, function, metabolic syndrome, hypertension, adiponectine

INTRODUCTION

There is an increasing incidence of life-style related diseases such as obesity, hyperlipidemia, hypertension and obesity and cancer worldwide. It is also noted that quantity and quality of dietary lipids could be important modulators associated with the morbidity and mortality of these diseases.[1-4] There has been recent developments with regard to functional lipids to promote health and prevent diseases.[5,6] In this review we examine how functional lipids, such as conjugated linoleic acid (CLA) and phospholipids (PLs), prevent the development of the metabolic syndromes.

HEALTH BENEFITS OF CONJUGATED LINOLEIC ACID

Antiobesity effect of CLA. Conjugated linoleic acids (CLA) that are found in dairy products and ruminant meats have attracted considerable attention because of their beneficial biological effects in attenuating diseases.[7] We have previously reported that the supplementation of CLA reduces abdominal white adipose tissue weights, serum triacylglycerol (TAG) levels, and liver TAG levels compared with a control diet in obese model Otsuka Long-Evans Tokushima Fatty (OLETF) rats.[8-11] These effects were attributed to enhanced fatty acid beta-oxidation and the suppression of fatty acid synthesis in the liver.[10] We have also reported that CLA enhanced fatty acid beta-oxidation in brown adipose tissue (BAT) and muscles and increased oxygen consumption and energy expenditure in rats.[11,12] Evidence also demonstrated that individual isomers of CLA have specific physiological functions on lipid metabolism.[12-15] We have reported that the 10t,12c-CLA isomer reduces the secretion of apolipoprotein B100 in cultured human hepatoma HepG2 cells and induces the hypolipidemic effect through the promotion of energy metabolism in OLETF rats.[12,13] The body fat-lowering effect of CLA has also been reported in humans.

Hypotensive effects of CLA. To date, a substantial amount of research has evaluated the effect of CLA on lifestyle-related diseases. However, no studies have evaluated the effect of CLA on hypertension.[16]

Epidemiologic studies have demonstrated an association between body mass index and blood pressure, and suggests that obesity is a risk factor for the development of hypertension in humans. To examine whether CLA could affect blood pressure, we conducted 2 different animal studies. In the first study, we evaluated the effect of CLA on the development of obesity-related hypertension in obese,

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diabetic Zucker rat.

Results show that feeding a CLA mixture (1% diet) alleviated hyperinsulinemia, and prevented the development of hypertension in Zucker rats.[17] This effect was attributed to the enhancement of plasma adiponectin levels through up-regulated mRNA expression in adipose tissue. CLA alleviated the metabolic syndrome through regulation of cytokine production in the liver and muscles of Zucker rats.[18,19] In another study, we evaluated the effect of a CLA isomer on the development of hypertension during the onset of obesity in OLETF rats. The 10t,12c isomer of CLA (0.5% diet) suppressed the development of hypertension by lowering the secretion of hypertensive adipocytokines, such as leptin and angiotensinogen in abdominal adipose tissue of OLETF rats.[20] Therefore, we concluded that CLA, especially its 10t,12c isomer, could prevent the development of obesity-related hypertension.

Presently, most hypertensive patients have emerged essential or secondary hypertension, whose specific causes remain unclear because of complex interactions between genetic predisposition and environmental factors. Spontaneously hypertensive rats (SHR) are one of the experimental models widely used in essential hypertension studies. We evaluated the effect of CLA on the development of essential hypertension in non obese SHR. Results show that administering the CLA mixture (1% diet) prevented the development of essential hypertension in SHR. The effect was attributable to the increase of plasma adiponectin level and the alleviation of membrane abnormality in SHRs.[21] This is the first time that the hypotensive effect of CLAs and its isomer has been demonstrated. In addition, the present study demonstrated the striking ability of CLA to regulate the production of physiologically active adipocytokines. Thus, CLA as a dietary adiponectin inducer may be useful in the alleviation of lifestyle-related diseases.[22]

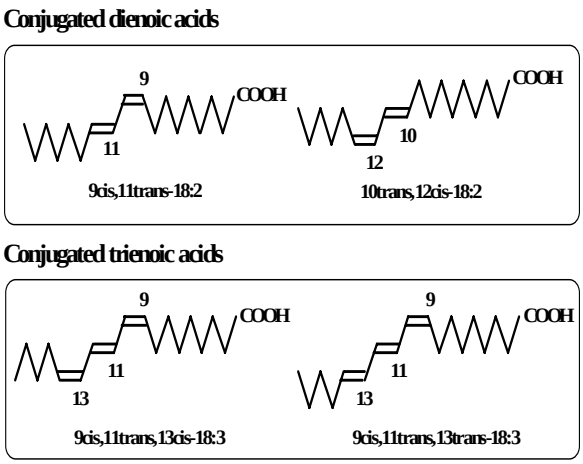

Figure 1. Structures of major conjugated fatty acids

PHYSIOLOGICAL FUNCTIONS OF DIETARY PHOSPHOLIPIDS

Dietary lipid contains 10% phospholipids (PL), It is estimated that the daily intake of dietary PL is around 3-4 g/day which or 5-8 % of the total lipid intake in the Japanese and other populations. PL can provide energy and are a source for polyunsaturated fatty acids (PUFA), such as arachidonic acid, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which may play an important role in growth and brain development as well as in the retinal photoreceptor cells. Furthermore, PL is a major component of cell membranes, and therefore, is important in nutritional and signal transduction for metabolic regulation, and maintenance of living cells. To date, many studies are in process to evaluate PL functions in the cells. However, there is only a limited amount of information available on the physiological functions of dietary PL. We previously reported that dietary phosphatidylcholine (PC) alleviated fatty liver through the suppression of hepatic lipogenesis in orotic acid administrated rats.[23] Recently, we also showed that omega3-PC from salmon roe, a rich source of EPA and DHA, prevented the development of obesity-related diseases through the suppression of lipogenic gene expressions and the enhancement of lypolytic gene expressions in the liver of obese rats.[24] It is of interest to determine whether the physiological effects of PL are the result of the polar head groups or the constituting PUFAs.

Few nutritional functions of other minor PLshave been identified thus far. To determine the possible nutritional and therapeutical use of minor PLs, by-products of food processing, the evaluation of the nutritional significance of these PL are required. Growing evidence has indicated that dietary PLs have lipid-lowering functions. Our previous study showed that Dietary phosphatidylinositol (PI) has lipid-lowering effects in the plasma and liver, and was associated with the inhibition of TAG synthesis through the suppression of diacylglycerol acyltransferase and phosphatidate phosphohydrolase activities in mice. It also inhibited phospatidylcholine synthesis by inhibiting ER-membrane-bound cytidylyltransferase activity.[25] Very recently, we found that dietary PI alleviated metabolic syndrome in Zucker rats. The effects were attributable to an increase in serum adiponectin, enhancement of fatty acid beta-oxidation and suppressed mRNA expression of inflammatory genes in the liver. (unpublished data)

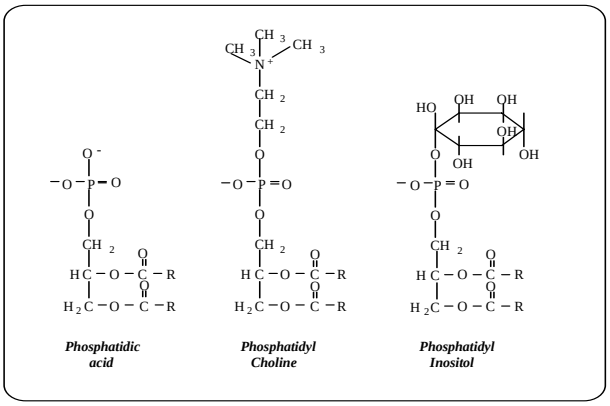

Figure 2. Structures of major phospholipids

AUTHOR DISCLOSURES

Teruyoshi Yanagita and Koji Nagao, no conflicts of interest.

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