Oat attenuate non-alcoholic fatty liver and obesity via inhibiting lipogenesis in high fat-fed rat

Chiung-Huei Peng[a,1], Hong-Chou Chang[b,1], Mon-Yuan Yang[c], Chien-Ning Huang[b,d], Shing-Jung Wang[e], Chau-Jong Wang[c,f,]*

[a]*Division of Basic Medical Science, Hungkuang University, Number 34, Chung Chie Road, Shalu County, Taichung 433, Taiwan*
[b]*Institute of Medicine, Chung Shan Medical University, Number 110, Section 1, Chien-Kuo North Road, Taichung 402, Taiwan*
[c]*Institute of Biochemistry and Biotechnology, Chung Shan Medical University, Number 110, Section 1, Chien-Kuo North Road, Taichung 402, Taiwan*
[d]*Department of Internal Medicine, Chung Shan Medical University Hospital, Number 110, Section 1, Chien-Kuo North Road, Taichung 402, Taiwan*
[e]*Division of Research and Development, STANDARD Foods Co., Taiwan*
[f]*Department of Medical Research, Chung Shan Medical University Hospital, Number 110, Section 1, Chien-Kuo North Road, Taichung 402, Taiwan*

ABSTRACT

Obesity accompanied with metabolic disorder is often complicated by hepatic regulations of lipid metabolism and lipoprotein recruitment. Recent reports have suggested that oat has metabolic-regulating effect. In this study, we examined whether oat could improve obesity, body fat, serum parameters and liver lipid metabolism. In high-fat-diet (HFD)-fed rats, oat effectively reduced body weight and fat, and decreased food efficiency but not appetite. Oat lowered serum glucose, free-fatty-acid (FFA), triacylglycerol (TG), cholesterol, and LDL-C/HDL-C elevated by HFD, and dose-dependently reduced hepatic TG and cholesterol. Thirty percent oat markedly reduced lipid synthesis biomarkers FAS, GPAT and HMG CoA reductase, while 15% and 30% oat stimulated expressions of oxidation markers PPARα, CPT-1 and phosphorylated-AMPK. Oat increased LDL receptor, being beneficial for serum lipid-lowering. Thus, Oat could act as adjuvant therapeutics for metabolic disorders via attenuating obesity, body fat, and improving serum parameters with metabolic regulation and lipid clearance of liver.

© 2012 Elsevier Ltd. All rights reserved.

1. Introduction

Obesity and body fat deposition play a critical role in the pathogenesis of metabolic disorders, including metabolic syndrome and cardiovascular disease (Calle, Thun, Petrelli, Rodriguez, & Heath, 1999). There is a metabolic link between the expanded body fat, high triacylglycerol (TG), high low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C) and insulin resistance, which leads to impaired metabolic regulation in adipose tissue and flux of free fatty acids (FFA) (Despres, 2006). Such flux of FFA toward the liver results in TG accumulation and secretion of

TG-rich lipoproteins, which in turn affects the distribution of lipoprotein subtypes and the activity of lipolipase.

Liver plays an essential role in regulating plasma lipid level through LDL clearance and HDL recruitment, while lipid uptake must affect the hepatic fat composition and thus burden the liver function. Non-alcoholic fatty liver disease (NAFLD) is generally considered as liver component of the metabolic syndrome, which is defined by hyperglycemia, obesity, hypertension and dyslipidemia (Friis-Liby, Aldenborg, Jerlstad, Rundström, & Björnsson, 2004). The regulation of hepatic lipid metabolism per se, including both lipogenesis and lipolysis, should be emphasized for preventing dislipidemia and the accompanying illness. Fatty acid synthase (FAS), glycerol-3-phosphate acyltransferase (GPAT), and 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG CoA) reductase, the committed enzymes regulating fatty acid, TG and cholesterol synthesis, were indicated as markers of lipogenesis (Thomas & Poznansky, 1990; Yang et al., 2010). On the other hand, the expressions of carnitine palmitoyltransferase-1 (CPT-1) and peroxisome proliferator-activated receptor α (PPARα) were critically associated with the process of lipolysis (Yang et al., 2010). Many studies have suggested that AMP-activated protein kinase (AMPK) plays an important role in lipid metabolism. Alpha-lipoic acid increased AMPK phosphorylation in the liver cells, thus preventing SREBP-1c expression and the development of NAFLD (Park et al., 2008). The activation of AMPK reduced the fat storage while also increasing fatty acid oxidation and the exocytosis of lipoprotein (Puljak et al., 2008).

Oat bran decreased the total cholesterol level in serum, and decreased the cholesterol and TG contents in the liver (Grajeta, 1999). Compared with the other gums, oat effectively reduced both the serum and hepatic lipids (Oda et al., 1994). The whole-grain oat cereal reduced LDL-C more than the low-fiber foods for adults with overweight and obesity (Maki et al., 2010). Oat-derived beta-glucan increased HDLC, while diminished LDLC and non-HDL cholesterol levels in overweight individuals with hypercholesterolemia (Reyna-Villasmil et al., 2007). It was reported that high beta-glucan-contained oat bran and oat gum, reduced postprandial serum glucose and insulin in both the control and type 2 diabetic subjects (Braaten et al., 1994). In streptozotocin-induced diabetic mice, oat significantly decreased fasting blood glucose, glycosylated protein, and free fatty acid content, while inhibited pancreatic apoptosis (Shen, Cai, Dong, & Hu, 2011).

Based on the previous reports that oat has metabolic regulating effect, in this study we aimed to examine whether oat could attenuate obesity and body fat deposition, as well as to improve serum glucose and lipid profile. The hepatic regulation of lipid synthesis, oxidation, and clearance was also investigated.

2. Materials and method

2.1. Animal experiment

Sprague–Dawley (SD) rats (weight 150 ± 10 g) were purchased from the National Laboratory Animal Breeding and Research Center (Taipei, Taiwan). Rats were housed and acclimated in laboratory conditions (23 ± 2 °C, 60 ± 5% relative humidity, and 12 h light/dark cycle) for at least 1 week before each study. Rats were fed with different diets and divided into the following groups ($n = 10$ per group): (A) standard chow (control), (B) high fed diet (HFD), (C) 92.5% HFD + 7.5% oat, (D) 85% HFD + 15% oat, and (E) 70% HFD + 30% oat. The ingredients contained in 1 gram (g) of whole oat are reported as: carbohydrate, 0.67 g; protein, 0.13 g; lipid, 0.08 g; fiber, 0.10 g; and β-glucan, 0.04 g (Wang et al., 2011). The composition of HFD diet was as follows (g/100 g food): beef tallow, 40; casein, 26; corn starch, 15; sucrose, 9; cellulose, 5; mineral mixture, 4; and vitamin mixture, 1. Mineral and vitamin mixtures, as described in AIN-93 (Reeves, 1997), were purchased from Oriental Yeast (Tokyo, Japan). The metabolized energy of the control and HFD-fed rats, with or without oat supplement, were 3.85 and 5.60 kcal/g, respectively. All rats, except the control group, were fed with HFD for 4 weeks. When confirmed their weight was 20% higher than the control, HFD rats were fed with the assigned diets, divided into groups B–E accordingly as mentioned above for another 8 weeks. All rats were weighed every week. The food intake of each rat was controlled equal as possible. The calculation of food efficiency = [weight increase (g)/total food intake (g)] × 100%.

All animal experimental protocols used in this study were approved by the Institutional Animal Care and Use Committee of the Chung Shan Medical University (IACUC, CSMU), Taichung, Taiwan (IACUC Approval No:885). After the end of the experiments, all animals were sacrificed. Blood samples and liver tissue were collected. Serum was prepared and stored at −80 °C for further investigations which was completed within 2 weeks.

2.2. Serum biomarkers

The serum sample was collected using ethylenediaminetetraacetic acid (EDTA) tubes and centrifuged at 3000 rpm (1400g) for 10 min at 4 °C. Concentrations of glucose, TGs, total cholesterol, LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), FFA, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine, ketone bodies, serum sodium and potassium were measured by enzymatic colorimetric methods using commercial kits (Randox Laboratories, Ltd., Antrim, UK). The analysis of serum was carried out by an automatic analyzer (Olympus AU2700, Olympus Co., Tokyo, Japan).

2.3. Determinations of total cholesterol and tg in liver

Livers were extracted from the animals and used for analyzing their lipid content. Briefly, liver (1.25 g) was homogenized with 10 mL of chloroform/methanol (1:2, v/v), and then thoroughly mixed with chloroform (1.25 mL) and distilled water (1.25 mL). After centrifugation (1500g for 10 min), the lower clear organic phase solution was transferred into a new glass tube and then lyophilized. A total of 0.1 g of lyophilized powder was dissolved in 1 mL of chloroform/methanol (1:2, v/v) as the liver lipid extract and stored at −20 °C for less than 3 days. The liver cholesterol and TGs in the lipid extracts were measured by enzymatic colorimetric methods using commercial kits (Randox Laboratories, Ltd., Antrim, UK).