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# Oat products modulate the gut microbiota and produce anti-obesity effects in obese rats

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ABSTRACT

Three oat products were supplemented into high fat diets and fed to obese rats for 8 weeks. Each oat product decreased body weight, epididymal fat accumulation, and serum inflammatory factor levels and significantly regulated serum lipid levels. Oat bran significantly reduced mean adipocyte size and TNF-α mRNA expression levels. Principal components analysis showed that the oat products shifted the overall structure of gut microbiota in DIO rats. The relative abundances of *Bacteroidetes* and *Firmicutes* and the *Bacteroidetes/Firmicutes* ratio were altered towards that of normal rats. Spearman's correlation analysis showed that changes in the overall microbiota composition were significantly correlated with total cholesterol, triacylglycerol, endotoxin, and tumour cell necrosis factor-α levels in serum, and mRNA expression levels. Oat products significantly increased the total short-chain fatty acids (SCFA) concentration in colonic digesta. These results suggest that oat products attenuate obesity and related metabolic disorders while modifying the gut microbiota composition in high fat diet-induced obese rats.



## 1. Introduction

Obesity is a major risk factor for several chronic metabolic disorders, such as dyslipidaemia, hypertension, and type II diabetes (Brown, Higgins, & Donato, 2000; Cani, Bibiloni, & Knauf, 2008). Increasing evidence suggests that dysbiosis of the gut microbiota plays a key role in the development of obesity. Previous studies reported that energy harvesting was positively associated with the number of *Firmicutes* in the intestine and negatively associated with the number of *Bacteroidetes* (Turnbaugh, Ley, & Mahowald, 2006). In addition, a reduction of beneficial bacteria and an increase in pro-inflammatory/pathogenic bacteria are consistently associated with the development of systemic inflammation (Veiga, Gallini, & Beal, 2010) and metabolic comorbidities (Zhang, Zhang, & Wang, 2010). Previous studies

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*Abbreviations:* HFD, high fat diet; NC, normal controls; MC, model controls; OM, oat meal; OF, oat flour; OB, high fibre oat bran; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PYY, peptide YY; LPS, lipopolysaccharide; LI, Lee's index; SCFA, short chain fatty acid; ET, endotoxin; IL-6, interleukin-6; TNF-α, tumour cell necrosis factor-α; OTUs, operational taxonomy units; PCA, principal component analysis

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showed that the composition and metabolism of gut microbiota were strongly influenced by eating habits (Scott, Duncan, & Flint, 2008). In summary, high fat diets (HFD) induce gut microbiota dysbiosis and should be targeted as an effective approach to obesity and related chronic metabolic disorder therapy (Wang, Tang, & Zhang, 2015).

Oat products have attracted attention for their considerable health benefits, such as weight-loss, reduction in postprandial glycaemia and reduction in serum low-density lipoprotein cholesterol (LDL-C) (Guevara-Cruz, Tovar, & Aguilar-Salinas, 2012; Maki, Beiseigel, & Jonnalagadda, 2010; Shen, Cai, & Dong, 2011). These physiological benefits are generally attributed to β-glucan, which is a non-starch polysaccharide composed of (1→3) and (1→4) linked β-D-glucopyranosyl units in varying proportions. β-Glucan is indigestible by human enzymes in the small intestine and is a prebiotic to promote bacteria growth (Shen, Dang, & Dong, 2012). Previous reports identified that oat β-glucan increase populations of beneficial bacteria (for example, *Lactobacillus* and *Bifidobacterium*) and decreases populations of pathogenic bacteria (for example, *Enterobacteriaceae*) both *in vivo* (Shen et al., 2012) and *in vitro* (Simon, Peter, & Glenn, 2007). In our daily life, our diet consists of oat products, rather than purified β-glucan. Despite these advances, the effects of oat products processed by different methods on the overall structure of gut microbiota and the relationship between these modulating effects and improvements in obesity-related metabolic disorders are poorly understood.

Most published studies on prebiotics in subjects with metabolic disorders used culture-based or targeted molecular analyses (Everard, Belzer, & Geurts, 2013; Wang et al., 2015). Variations in microbiota composition were generally evaluated by changes in certain bacteria (Snart, Bibiloni, & Grayson, 2006). There is limit studies on the complete profile of oat product-induced alterations in gut microbiota, because bacteria that cannot be cultured and those that share low homology with the specific probes/primers utilized remain unidentified (Wang et al., 2015). Recent developments in metagenomic sequencing represent a powerful alternative to rRNA sequencing for analysing complex microbial communities (Riesenfeld, Schloss, & Handelsman, 2004).

In this study, we compared the effects of oat meal (OM), oat flour (OF) and high fibre oat bran (OB) on host lipid metabolism and gut microbial community structure in diet-induced obese (DIO) rats. Body weight, epididymal fat accumulation, serum lipid levels, serum inflammatory factors, tumour necrosis factor α (TNF-α) mRNA expression levels in liver and adipose tissue and colonic short-chain fatty acid (SCFA) concentrations were tested during this experiment. Histomorphological changes in adipose tissue were also observed. Furthermore, gut microbiota composition was characterized using Illumina HiSeq sequencing technology.

## 2. Materials and methods

### 2.1. Chemicals

The total starch assay kit, total dietary fibre assay kit, mixed-linkage beta-glucan assay kit and resistant starch assay kit were purchased from Megazyme International Ireland Ltd. (Bray, Ireland). Commercial biochemical assay kits for triacylglycerol (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were purchased from BioSino Bio-technology and Science Inc. (Beijing, China). Commercial ELISA assay kits for endotoxin (ET) and tumour cell necrosis factor-α (TNF-α) were purchased from Nanjing Jiancheng Bioengineering Institute (Nanjing, China). The E.N.Z.A. ®Stool DNA isolation kit was purchased from Omega Bio-Tek Inc. (Doraville, CA, USA). Acetic acid, propionic acid, iso-butyric acid, butyric and crotonic acid standards were purchased from Sigma Inc. (St. Louis, MO, USA). Formalin, haematoxylin, and other chemicals were analytical reagent grade.

### 2.2. Materials

OM, OF and OB were commercial products purchase from Jinlvhe Biotechnology Co., Ltd (Shanxi, China). The following nutritive components were analysed: total dietary fibre (AOAC) method 985.29, total β-glucan content (AOAC) method 995.16, crude protein (Kjeldahl Method), crude fat (Soxhlet abstracting method), crude ash (Combustion method), total starch (AOAC) method 991.43, moisture content (Constant weight method) and resistant starch content (AOAC) method 2002.02 from the three oat products. The physicochemical characteristics, including water-retaining capacity and swelling capacity, were also determined using the methods previously described by Wang, Li, and Jiao, 2009. The apparent viscosity was measured with an NDJ-1 rotating viscometer (Hengping Scientific, Shanghai, China) at specific conditions (25 °C, 5% M/M, 200 rpm) (Xu, Zhou, & Wang, 2012). β-Glucan samples were prepared in a two-step method with ethanol-enzymatic and water from the three oat products according to the method by Shen et al. (2012). Purification of β-glucans was performed with ion-exchange chromatography on DEAE-Sepharose CL-6B and gel chromatography on Sepharose CL-4B. The average molecular weights ($M_w$) of the three β-glucans samples were measured using a high performance size elusion chromatography coupled with multi angle laser light scattering and refractive index (HPSEC-MALLS-RID) system. Samples were filtered on a 0.45-μm membrane before injection (100 μL) and eluted with 0.1 M NaCl (0.5 mL/min). The column temperature was kept at 40 °C (Liu, Xu, & Zhang, 2012).

### 2.3. Animals and experimental diets

After 7 days acclimatization, 80 male Sprague-Dawley rats (4 weeks of age, weighing 135 ± 10 g, obtained from the Laboratory Animal Centre of Henan Province, Zhengzhou, China, SCXK: 2010-0002) were randomly divided into two groups. The normal control (NC) group (containing 10 rats) was fed normal chow, and the other group (containing 70 rats) was first fed a high-fat diet to establish a diet-induced obesity model (DIO, the average body weights were more than 120% compared with normal rats). After 6 weeks of this modelling, 40 DIO rats were randomly subdivided into four groups (10 rats per group). One group was maintained on the HFD as model controls, and the other three groups were fed HFD supplemented with oat products (OM, OF and OB) with the same amount of β-glucan [0.70 g/(kg•BW•d)] for 8 weeks. Rats had free access to water and food during this period. Food intake was recorded at 0, 3, and 6 w,