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Supplement of bamboo extract lowers serum monocyte chemoattractant protein-1 concentration in mice fed a diet containing high level of saturated fat

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Abstract

Monocyte Chemoattractant Protein-1 (MCP-1) is an inflammatory chemokine upregulated in obese subjects contributing to the development of type 2 diabetes. This study investigated the inhibitory effect of an ethanol/water extract from bamboo *Phyllostachys edulis* (BEX) on blood concentration of MCP-1. C57BL/6J mice were fed standard or high fat diet with or without BEX supplement (11 g dry mass per 17,000 kJ) for 6 months. Ten mice were used in each group. Body weight and food consumption were measured weekly. After euthanization, the weight of visceral fat and circulating MCP-1 concentration were measured. In comparison to the standard control group, the high fat control group increased body weight, abdominal fat storage, and serum MCP-1 concentration by 60% ($P<0.001$), 266% ($P<0.001$), and 180% ($P<0.01$), respectively. While the high fat BEX group showed a 3% decrease in body weight ($P<0.01$), 24% decrease in mesenteric fat depot ($P<0.01$), and 49% decrease in serum MCP-1 ($P<0.05$) in comparison to the high fat control group. This study suggests BEX supplement in the high fat diet ameliorates elevated MCP-1 concentrations in the blood, whether this is related to modulated endocrine properties of the visceral fat is to be studied.

Keywords

MCP-1; high fat diet; bamboo extract; mesenteric fat

Introduction

The monocyte chemoattractant protein-1 (MCP-1/ CCL2) is a member of the C-C - chemotactic cytokine (chemokine) family, produced by multiple cell types constitutively or after induction [1]. The circulating level of MCP-1 was found ~50% higher in obese mice [2] and in human subjects with type 2 diabetes [3] in comparison to controls. MCP-1 recruits monocytes into adipose tissues and enhances obesity-associated chronic inflammatory [4] and insulin resistance [5]; it also facilitates the expansion and remodeling of the adipose tissue during development of obesity through angiogenic effect on endothelial cells [6];

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furthermore, this chemokine can decrease the liposynthesis ability of adipocytes [2] and subsequently elevates the free fatty acid level in the circulation [4], exerting lipotoxicity in the periphery [7]. Therefore inhibiting MCP-1 overproduction has become a preventive strategy for obesity-induced type 2 diabetes.

Our previous study has shown that an ethanol/water extract from bamboo *Phyllostachys edulis* (BEX) efficiently protected murine muscle C2C12 cells from lipotoxicity [8], an obesity-related condition leading to inflammation and insulin resistance [9, 10]. In this study, it is further revealed that BEX as a dietary supplement significantly decreased the circulating level of MCP-1 in mice treated with a diet containing high level of saturated fat, with concurrence of decreased weight of mesenteric fat depot.

Experimental Methods

Bamboo extract (BEX)

The BEX used in this study was provided by Golden Basin LLC (Kailua, HI). It is made from fresh leaves and small branches of bamboo *Phyllostachys edulis* in Hunan Province, China, through a patented ethanol/water extraction procedure (Chinese invention patent, CN 1287848A).

Animals

Male C57BL/6J mice were purchased from Jackson laboratories (Bar Harbor, MN) at 4 weeks. The mice were housed 3–4 per cage, and had access to water and food *ad libitum*. The room temperature was controlled at 20°C and lighting was turned on and off with 12 h intervals. Institutional and national guidelines for the care and use of animals were followed and that all experimental procedures involving animals were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Hawaii.

Dietary treatment

After one week of acclimation with regular rodent chow, the mice were fed standard (10% energy from fat) or high fat (60% energy from fat) diet with or without BEX supplement (11 g dry mass per 17,000 kJ) for 6 months. Ten mice were used in each dietary group. Body weight and food consumption were measured weekly. All diets were purchased from Research Diets (New Brunswick, NJ, USA). The dietary composition is listed in Table 1.

Measurement of the abdominal fat pads

After euthanization, epididymal fat, perirenal fat, and mesenteric fat were collected and weighed.

Serum MCP-1 quantification

Blood was collected through cardiac puncture. MCP-1 concentrations in the sera were measured using Cytometric Bead Array (CBA) - Mouse MCP-1 Flex Set (BD Biosciences, Bedford, MA).

Statistical Methods

Software used were Prism 4.0a (GraphPad Software, Inc.) and Stata 11.0 (StataCorp LP). Statistical method used in Table 2 was two-way ANOVA with Bonferroni post hoc test; methods used to analyze the weekly record of body weight were linear regression with Huber correction and random effects regression to account for multiple measurements per mouse. $P = 0.05$ was considered statistically significant.

Results

Table 2 summarizes the major findings of this study. During the 6 months of treatment, the high dietary fat content increased the daily energy intake by approximately 30% ($P < 0.0001$). BEX supplement did not affect the energy intake. The body weight of the mice at both start and end points are shown. High fat diets resulted in an averaged 60% increase in body weight ($P < 0.0001$) at the endpoint. When the weekly record of the body weight (data not shown) was analyzed, BEX supplement in the high fat diet was found to slightly decrease (-3% , $P < 0.01$) the weight gain of the mice.

The high dietary fat content also increased the total weight of the abdominal fat by ~3 folds. When the weight of individual fat depot was analyzed, BEX was found to increase the epididymal fat by 20% (0.37 g, $P < 0.05$), and decrease mesenteric fat by 24% (0.52 g, $P < 0.01$), but did not affect the total weight of the visceral fat. An interaction between the fat content and BEX was found in regulating the weight of the mesenteric fat depot ($P < 0.01$).

Most interestingly, BEX supplement dramatically decreased high fat diet-induced elevated MCP-1 concentration in the serum (-49% , $P < 0.05$), and whether this is related to modulated endocrine properties of the visceral fat, especially the mesenteric fat, is to be studied.

Discussion

Using the same diet containing high level of saturated fat, Yu et al. (2006) [11] treated C57BL/6 mice for 3 months, and compared MCP-1 expression and secretion in four types of adipose tissues: mesenteric, epididymal, perirenal, and subcutaneous. While the amounts of MCP-1 protein released by epididymal, perirenal, and subcutaneous fat depots were about the same, this level quadruplicated in the mesenteric fat. Mesenteric adipose tissue-conditioned medium also induced the highest degree of macrophage migration and stimulated pro-inflammatory cytokine production in macrophages. These findings indicate that in comparison to other fat depots, the mesenteric fat tissue has a more pronounced role in obesity-associated inflammation. Our study showed that BEX supplement in high fat diet decreased the weight of mesenteric fat by 0.52 g, and therefore it may attenuate MCP-1 secretion from this tissue and subsequently contribute to the decrease of MCP-1 in the circulation. Although BEX increased the weight of epididymal fat by 0.37 g, this may not compensate the change caused by the mesenteric fat due to the dramatic difference between the MCP-1 secretion abilities of these two fat depots. This suggests that BEX may later the distribution of fat storage in the visceral adipose tissues and lower MCP-1 secretion as a final result. Although white adipose tissue is a major source of MCP-1[2], this chemokine is

also produced in other tissues [12–14], and therefore a systematic study is needed to evaluate the tissue-specific effect of BEX.

Other natural products that inhibit the overproduction of MCP-1 in obese/diabetic rodents and in cell culture models include traditional Asian medicine [15–18], extracts from herbs [19], spices [20, 21], fruits and vegetables [22–25]. Due to the use of different models and experimental procedures, and variable purity of the extracts, it is difficult to perform accurate comparison between the efficacy of BEX and other reported natural products. The daily dose of BEX used in this study was 773 mg/kg body weight for mouse, and this corresponds to 63 mg/kg body weight for human (3.8 g per day for a 60 kg adult) when the body surface area normalization method is used for an allometric dose translation [26].

BEX used in this study consists of approximately 50% water, 20% saccharides, 10% protein, and 20% other components. The active component(s) contributing to the effects described above are to be further determined. The extraordinary abundance of the raw material is a major advantage of this natural product. *Phyllostachys Edulis* is known for its fast growth, wide geographical distribution and easy propagation. The raw materials (small branches and leaves) used for BEX production are by products of the bamboo timber industry. Therefore the present study suggests a potential nutraceutical application of a rich and environmental-friendly natural resource.

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Table 1

The composition of the diets used in this study.

Diet	Standard control		Standard BEX		High fat control		High fat BEX	
	g	kJ	g	kJ	g	kJ	g	kJ
Casein, 80 Mesh	200	3349	200	3349	200	3349	200	3349
L-Cystine	3	50	3	50	3	50	3	50
Com Starch	315	5275	315	5275	0	0	0	0
Maltodextrin 10	35	586	35	586	125	2093	125	2093
Sucrose	350	5862	350	5862	68.8	1151	68.8	1151
Cellulose, BW200	50	0	50	0	50	0	50	0
Soybean Oil	25	942	25	942	25	942	25	942
Lard	20	754	20	754	245	9232	245	9232
Mineral Mix S10026	10	0	10	0	10	0	10	0
DiCalcium Phosphate	13	0	13	0	13	0	13	0
Calcium Carbonate	5.5	38	5.5	38	5.5	38	5.5	38
Potassium Citrate, 1H2O	16.5	0	16.5	0	16.5	0	16.5	0
Vitamin Mix V10001	10	167	10	167	10	167	10	167
Choline Bitartrate	2	0	2	0	2	0	2	0
Bamboo Extract (dry mass)	0	0	11	0	0	0	11	0
Water from Bamboo Extract	0	0	11	0	0	0	11	0
FD&C Yellow Dye #5	0.05	0	0.025	0	0	0	0.025	0
FD&C Red Dye #40	0	0	0	0	0	0	0.025	0
FD&C Blue Dye #1	0	0	0.025	0	0.05	0	0	0
Total	1055.1	16986	1077.1	16986	773.9	16986	795.9	16986

Table 2
Energy intake, body weight, abdominal fat, and serum MCP-1 concentration in the mice

Energy intake is the average of the weekly measurements. Average (SD) are shown. Values in the same row without a common letter differ.

Group ID	Standard control	Standard BEX	High fat control	High fat BEX
Energy intake (kJ/day)	39.4 ^a (4.0)	37.9 ^a (4.5)	50.3 ^b (5.3)	50.9 ^b (3.6)
Body weight (g) (Start)	17.8 ^a (2.1)	18.2 ^a (1.8)	18.0 ^a (0.9)	18.4 ^a (1.1)
Body weight (g) (End)	28.7 ^a (3.1)	28.3 ^a (2.5)	47.5 ^b (2.2)	44.6 ^b (2.6)
Epididymal fat (g)	0.65 ^a (0.26)	0.78 ^a (0.38)	1.84 ^b (0.24)	2.21 ^c (0.37)
Perirenal fat (g)	0.17 ^a (0.07)	0.24 ^a (0.16)	0.85 ^b (0.31)	0.74 ^b (0.19)
Mesenteric & omental fat (g)	0.22 ^a (0.08)	0.30 ^a (0.14)	2.17 ^b (0.23)	1.65 ^c (0.47)
Total abdominal fat (g)	1.04 ^a (0.38)	1.32 ^a (0.66)	4.86 ^b (0.58)	4.69 ^b (0.39)
Serum MCP-1 (pg/ml)	16.26 ^a (6.58)	19.34 ^a (3.23)	45.78 ^b (9.56)	23.37 ^a (1.75)

BEX, bamboo extract