The Effect of Gum Arabic on Energy Balance Genes in Mouse Liver

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Authors’ contributions
This work was carried out in collaboration between all authors. Authors JSF, HHM and AAA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors AZS and THM managed the analyses of the study. Author HHM managed the literature searches. All authors read and approved the final manuscript.

ABSTRACT

Aims: Energy homeostasis is regulated by a complex neuroendocrine system including appetite regulatory hypothalamus peptides and adipocytes derived peripheral signals. The aim was to study the effects of Gum Arabic on fat mass and obesity-associated gene expression in liver.

Study Design: This case control study was conducted at Key laboratory of Biochemistry, Nanjing Agricultural University, China.
Methodology: Female C57BL/6 J mice at 13 weeks of age were treated with 10% of gum Arabic in drinking water for 12 weeks. Food intake, body weight, visceral adipose tissue (VAT), blood glucose and lipids profiles were measured. The expression of energy balance related genes was measured by Real-time PCR.

Results: Gum Arabic significantly (P<0.05) decreased food intake, body weight, and VAT accumulation. Gum Arabic significantly (P<0.05) decreased blood glucose, total cholesterol, and LDL-c, whereas increased high-density lipoprotein (HDL). Gum Arabic had no significant effect on the expression of neuropeptide Y (NPY), adenosine monophosphate (AMP), agouti (Ago) protein and fat mass and obesity-associated protein (FTO) in the liver.

Conclusion: Gum Arabic had significant effect on food intake, body weight and VAT associated with decreased blood glucose and lipid profiles, without any change in the expression rate of energy homeostasis genes.

Keywords: Gum Arabic; gene expression; energy balance genes; mice.

1. INTRODUCTION

Obesity is a state of increased abdominal fat deposition consequential from chronic nutrient intake, where energy intake exceeds energy expenditure [1]. Energy expenditure was influenced by basal metabolism rate [2], physical activity [3], body size and lifespan [4], and thermogenesis [5]. Disturbances of central [6] and peripheral [7] signals may lead to obesity and anorexia. Obesity poses a risk factor for hypertension, diabetes, hyperlipidemia, cancer and other metabolic disorders. In addition, obesity regulates food intake, appetite and fat deposition [8]. Energy homeostasis is regulated by a complex neuroendocrine system including appetite regulatory hypothalamic peptides [9], adipocytes-derived peripheral signals such as leptin [10]. These signals are integrating information about energy status [11]. Among all the cerebral circuits involved in the regulation of feeding behavior and energy balance, the hypothalamus seems to play a significant role in the orchestration of several neurotransmitters essentials to the fine tune of these behaviors [12].

A variety of orexigenic and anorexigenic neuropeptides have played a critical role in food intake and energy balance [13]. For instance, orexigenic neuropeptides include orexin (ORX) [14], agouti protein (Ago) [15] and neuropeptides Y (NPY) [16] after, and anorexigenic neuropeptides such as corticotropin releasing hormone (CRH) [17], proopiomelanocortin (POMC) [18], glucagon-like peptide-1(GLP-1) [19], and AMP activated protein kinase (AMPK) [20] control food intake. However, previous study has indicated that FTO has a significant effect on body mass index (BMI) and increased food intake [21]. In addition, others studies showed that hypothalamic expression of NPY, FTO, POMC, AMP, and Ago have an important role in food intake and energy homeostasis [9,22].

Gum Arabic is edible dried sticky exudates rich in soluble fiber. It is used in food and pharmaceutical industry as an emulsifier and preservative [23]. Studies showed that a high ingestion of dietary fiber, including Gum Arabic, is associated with beneficial effects on fat metabolism [23,24]. Dietary fiber can manage body weight by altering glycaemic index and affecting gastric and gut hormone secretion [25].

Recently, the effect of Gum Arabic on the expression of lipid metabolism genes was studied [26]; effects on the reduction of abdominal fat accumulation and its association with the downregulation of 11β-hydroxysteroid dehydrogenase expression have been reported in mice liver and muscle [27]. The aim of this study was to determine the effect of Gum Arabic on energy balance related genes expression in the liver of mice.

2. MATERIALS AND METHODS

2.1 Experimental Animals

This is a case control study conducted in the Key laboratory of Biochemistry, Nanjing Agricultural University, China. Gum Arabic used in this study was from Acacia Senegal tree from Sudan. Twenty female C57BL/6 J mice at 13 weeks of age were housed in plastic cages (each containing five mice) kept in a room at 25°C with a 12hr light and dark cycle. The mice were allowed free access to a commercial pelleted diet for the adaptation and drinking water throughout the experiment. After 3 days of acclimatization, the mice were divided into control and gum
Table 1. Primers used for real-time PCR

<table>
<thead>
<tr>
<th>Target genes</th>
<th>PCR products (bp)</th>
<th>Primer sequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAPDH</td>
<td>300</td>
<td>F: 5'-ACATGGTCTACATGTTCAGTA -3'</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R: 5'-GGAGTCTACTGGTGCTTCA -3'</td>
</tr>
<tr>
<td>FTO</td>
<td>200</td>
<td>F: 5'-AGCAGAGCAGCTACAAC-3'</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R: 5'-CTGGACTGTCCTCACTTTT -3'</td>
</tr>
<tr>
<td>NPY</td>
<td>168</td>
<td>F: 5'-AGTTGATGAGTGTGGTGCGAGA -3'</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R: 5'-AGGTAACAAGCGAATGTTCA -3'</td>
</tr>
<tr>
<td>AMP</td>
<td>111</td>
<td>F: 5'-GCCGACTTTGGTCTTTCA-3'</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R: 5'-GCCTGCGTACAATCTTCC-3'</td>
</tr>
<tr>
<td>Agouti</td>
<td>186</td>
<td>F: 5'-TCCCAGGTCTAAGTCTGAGAATG -3'</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R: 5'-ACGGCTCGAGCGAGGTA -3'</td>
</tr>
</tbody>
</table>

FTO, fat mass and obesity-associated protein; NPY, neuropeptide Y; AMP, adenosine monophosphate

Arabian groups each with 10 mice. Gum Arabic mouse group received 0.5% of gum Arabic aqueous solution as drinking water for 7 days, and then 10% solution for the further 12 next weeks. The control group was given water through the experimental period. Body weight and food intake was measured during the experiment. In addition, fasting blood samples were collected from all mice. Then mice were killed at the end of the experiment, liver and visceral adipose tissues were dissected, weighed and stored at -80°C. The experimental procedures were approved by the Animal Ethics Committee of Nanjing Agricultural University (Nanjing, China).

2.2 Plasma Lipid Profile

Blood glucose, total cholesterol, triglyceride, HDL-c and LDL-c, were assayed using kits purchased from Nanjing Jiancheng Bioengineering Institute (Nanjing, China).

2.3 Gene Expression

About 100 mg of liver was ground in liquid N₂, and 50 mg was used for RNA extraction using TRIzol total RNA kit (Invitrogen, Biotechnology Co, Ltd, Carlsbad, CA, USA) according to the manufacturer's instruction. Complementary DNA was synthesized using Prime Script RT reagent kit according to the manufacturer's instruction (Takara). The effect of Gum Arabic on the expression of energy balance related genes in mice was detected using real-time PCR performed in Mx3000P (Stratagene, USA). Specific primers for NPY, FTO, Ago, and AMP (Table 1 above) were synthesized by Geneary (Shanghai, China). Mice GAPDH served as a reference gene for normalization purposes. The method of $2^{-ΔΔCt}$ was used to analyze the real-time PCR data [28,29,30].

2.4 Statistical Analysis

Data are expressed as the mean±SEM and compared by Student's t-test, $P<0.05$ was considered significant. All statistical analyses were performed using SPSS 16.0 software (SPSS, Chicago, IL, USA).

3. RESULTS

3.1 Body Weight and Food Intake

Gum Arabic significantly decreased body weight and food intake ($P<0.05$), and visceral adipose tissue accumulation ($P<0.01$), while has no significant effect on liver weigh ($P<0.05$) Fig. 1.

3.2 Plasma Lipid Profile

Gum Arabic significantly decreased ($P<0.05$) blood glucose, total cholesterol, and LDL-c. In addition, Gum Arabic significantly increased ($P<0.05$) the level of HDL-c, and had no significant effect on triglyceride Table 2.

3.3 The Expression of Energy Balance Related Genes

The results have shown that Gum Arabic had no significant effect on the expression of the energy balance related genes NPY, AMP, Ago protein and FTO in liver Fig. 2.

4. DISCUSSION

The obesity results from fast food consumption with poor dietary outcomes [31]. Obesity plays a significant role in the development of many diseases [32], such as, type 2 diabetes [33] and cancer [34]. Supplementation with Gum Arabic in drinking water significantly decreased body
weight and food intake. This may be because a high intake of dietary fiber, including Gum Arabic, was associated with beneficial effects on fat metabolism [23,24]. In addition, the dietary fiber was promoting satiety and satiation, altered glycaemic index, affects gastric emptying, stomach hormone secretion and reduces weight [25]. Moreover, Gum Arabic inhibits absorption of glucose in the intestine via interaction with membrane abundance of SGLT1 in mice [35].

Abdominal obesity is associated with metabolic syndrome [36], and metabolic syndrome is considered a fatal consequence of visceral obesity [37]. In the current study, Gum Arabic significantly decreased the accumulation of VAT in mice submitted to 10% of Gum Arabic in drinking water. Similarly, 1% of Gum Arabic in drinking water was reduced VAT [38]. Gum Arabic, dietary fiber may prevent obesity by several mechanisms for example via lowering caloric density of food [39], and/or decreasing fat absorption in the small intestine [40]. The reduction in the VAT mass may be a consequence of a lower caloric intake. Since a dietary fiber are believed to reduce food intake [39], after study soluble dietary fiber may have the potential effects to limit cholesterol and fat

![Fig. 1. The effect of gum Arabic on food intake (A), body weight (B), Liver weight (C) and VAT (D)](image)

The values are expressed as means ± SEM, n=10/group. Different superscript letters above the bars indicate significantly different mean values at P<0.05.

<table>
<thead>
<tr>
<th>Group</th>
<th>Glucose (mmol/L)</th>
<th>Triglyceride (mg/dL)</th>
<th>Total cholesterol (mg/dL)</th>
<th>HDL-c (mg/dL)</th>
<th>LDL-c (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>7.01±0.6a</td>
<td>37.5±3.1a</td>
<td>69.1±1.5a</td>
<td>55.4±1.4a</td>
<td>36.1±2.33a</td>
</tr>
<tr>
<td>Gum Arabic</td>
<td>3.52±1.5b</td>
<td>39.2±1.3a</td>
<td>49.4±1.4b</td>
<td>68.9±3.5b</td>
<td>24.2±2.5b</td>
</tr>
</tbody>
</table>

HDL-c, high density lipoprotein; LDL-c, low density lipoprotein.
Different superscript letters above value indicate significantly different mean values at P<0.05.
Fig. 2. The effect of Gum Arabic on hypothalamic expression of orexigenic and anorexigenic neuropeptides genes

FTO (A); NPY (B); AMP(C); and Ago (D). The values are expressed as means ± SEM, n=6/group. Different superscript letters above the bars indicate significantly different mean values at P<0.05.

absorption as proposed previously [41]. Hypothalamic NPY signaling network plays significant roles in the regulation of energy balance [42]. The present study indicated that Gum Arabic doesn't effect the expression of NPY that regulate food intake and energy balance. Further study was needed using male mice to confirm the result since in this study only female mice were used, in which estrus cycle and behavior may effect the results.

5. CONCLUSION

The present study indicated that, in the liver, Gum Arabic doesn't affect the expression of energy balance related genes.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

ACKNOWLEDGEMENT

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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