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ORIGINAL ARTICLE

Gum Arabic supplementation improved antioxidant status and alters expression of oxidative stress gene in ovary of mice fed high fat diet

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Abstract Obesity is a global health concern associated with high morbidity and mortality. Therapeutic strategies include surgery and synthetic drugs, and may cause high costs and serious complications. Gum Arabic (GA, *Acacia senegal*) considered as a dietary fiber that reduces body fat deposition. Yet, the effect of the GA on reproductive functions in high fat diet remains unclear. In this study, we fed mice either a normal diet (control), low fat diet (low), high fat diet (high) or a high fat diet supplemented with 10% w/w GA (high + gum) for 12 weeks. Body weight, visceral adipose tissue (VAT), plasma lipid profile and blood glucose were determined. Ovarian antioxidant capacity was evaluated by the measurement of antioxidant enzymes, malondialdehyde (MDA) and antioxidant enzymes activity. Moreover, ovarian histopathological changes and oxidative stress related genes mRNA were measured. GA treatment significantly ($P < 0.05$) increased activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) compared to low, HFD and control groups. The treatment of GA significantly ($P < 0.05$) decreased ovary

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MDA, plasma total cholesterol, LDL-c and triglyceride concentrations whereas, increased HDL-c concentrations compared to low, HFD and control groups. SOD and GPx mRNA expression were significantly increased in GA group compared to low, HFD and control groups. Ovaries of all HFD mice showed marked degeneration whereas, slight degeneration was observed in GA treated mice compared to low, HFD and control groups. Our findings suggest that GA may protect ovaries by improvement of antioxidant capacity; thus, it may be useful to ameliorate the fertility complications in obese patient.

1. Introduction

The global increased infertility or sterility rates, particularly in industrialized countries have been a hotly debated issue (1), mainly on the relative contributions of metabolic diseases and obesity factors (2,3). Infertility is the most important clinical problem, affecting people psychosocially (4) and medically (5). In recent years, oxidative stress has been involved in the progression of male infertility (6). The experimental evidence has been implicated that these damaging processes are caused by free radicals (7). The deleterious effects of oxidative stress come from either an increased amount of reactive oxygen species (ROS) production (8,9) or a decrease of natural cell antioxidant capacity of an organism (10). However, the utilization of foods rich with antioxidant phytochemicals may reduce the deleterious effects caused by oxidative stress (11).

Oxidative stress (OS) is a condition characterized by inconsistency between pro-oxidant molecules including reactive oxygen species (ROS) and nitrogen species, and antioxidant defenses (12,13). Low levels of ROS play crucial role in many physiological processes such as normal reproductive performance (14), intracellular signaling (15), and apoptosis (16). However, high levels of ROS have been well-known to play major role in the pathogenesis of infertility in both females (17) and males (18). The harmful effects of OS on sperm functions and quality have been extensively studied (7,19). In females, the adverse effects of OS on reproductive functions remain unclear. This imbalance between pro-oxidants and antioxidants resulted in a number of reproductive diseases for example, polycystic ovary syndrome (20), endometriosis (21,22) and infertility (23). OS also induces pregnancy complications such as recurrent pregnancy loss (24), spontaneous abortion (25), and preeclampsia (26). Recent studies have revealed that extremes of body weight gain and lifestyle factors such as high caloric intake promote excess free radical production (27,28), which ultimately affects fertility (29). Supplementation of antioxidant may be valuable in reducing ROS production (30) and useful to be explored as a prospective strategy to overcome reproductive disorders associated with infertility (31–33). However, the effects of dietary fiber supplementation treatment of reproductive complication associated with obesity have not been reported.

Gum Arabic (GA) is an edible, dried sticky exudate from *Acacia seyal* and *Acacia senegal*, which is rich in non-viscous soluble fiber. It is commonly used in food industry and pharmaceutical field as an emulsifier and preservative (34). In the North Africa and Middle East, it has been used as an oral hygiene agent by various communities for centuries (35). GA is used in Arabic folk medicine to decrease both frequency and need of hemodialysis in patients suffering from chronic renal failure (36). It has strong antioxidant properties, and is used to reduce the experimental nephrotoxicity against gentamicin (36) and cisplatin (37) and to ameliorate cardiotoxicity (38). Moreover, GA is reported to reduce oxidative and inflammation against adenine induced chronic renal failure in rats (39) and improved the kidney functions in diabetic rat (40,41). However, the effects of GA on antioxidant capacity and reproductive functions in mice fed high fat diet have not been reported. Moreover, remained less clear whether GA can change ovarian oxidative stress enzymes activity and genes expression.

Therefore, in the present study, we used high fat diet mice model to test our hypothesis that supplementation of GA in drinking water may reduce the oxidative damage in the ovary, and the reduction of oxidative damage may associate with modulation of oxidative related genes expression in ovary.

2. Materials and methods

2.1. Animals

Eight-week-old female CD-1 mice were housed in a room at 23 ± 1 °C with a 12/12-h light–dark cycle. The animals had free access to water and standard mouse chow for an acclimatization period of 1 week. After that, animals weighing 23–24 g were randomly divided into four groups. The control group (n = 20) was fed standard mouse chow, low-fat diet (low, n = 20), high-fat diet (high, n = 20) and high-fat diet with GA groups (high with gum, n = 20). The food was purchased from Jiangsu Province Cooperative Medical and Biological Engineering Co. Ltd (Table 3). Body weight and food intake were recorded throughout the study. At the end of 12 weeks, the whole blood was collected from the orbital fossa into EDTA-containing tubes, and plasma was prepared by centrifugation at 3000 rpm for 15 min at 4 °C and stored at −80 °C until biochemical analysis. The mice then were killed by rapid decapitation. Ovary samples were dissected and weighed after a wash shortly in cold PBS (pH 7.4). The ovaries were immediately freezed in liquid nitrogen and stored at −80 °C until further analysis. The experimental procedures were approved by the Animal Ethics Committee of Nanjing Agricultural University (Nanjing, China).

2.2. Plasma biochemical analysis

Blood samples were collected in heparin coated tubes and plasma samples were obtained by centrifugation and kept at