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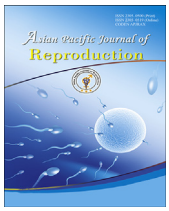

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Gum arabic improves semen quality and oxidative stress capacity in alloxan induced diabetes rats

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ABSTRACT

Objective: To explore effect of gum arabic (GA) on semen quality and oxidative stress capacity of alloxan induced diabetes rats.

Methods: In this study, male Sprague–Dawley rats were divided into 3 groups ($n = 20$ of each): control group, diabetic group which were injected with alloxan, and diabetic group which was given 10% GA in the form of drinking water for 10 weeks. The effect of GA on testicular oxidative stress and sperm quality were investigated. Testicular antioxidant was detected by the measurement of antioxidant enzymes, malondialdehyde in testis tissue. Moreover, plasma lipids, testis histopathological changes and oxidative stress related genes mRNA were evaluated.

Results: The treatment of GA significantly ($P < 0.05$) increased semen quality compared the diabetic and control groups. Similarly, the treatment of GA significantly ($P < 0.05$) increased the activities of catalase, superoxide dismutase and glutathione peroxidase compared to diabetic and control groups. The treatment of GA significantly ($P < 0.05$) decreased testis malondialdehyde, plasma total cholesterol, low-density lipoprotein cholesterol and triglyceride concentrations, whereas increased high-density lipoprotein cholesterol concentrations compared to the diabetic groups. Glutathione peroxidase and superoxide dismutase mRNA expression were significantly ($P < 0.05$) increased in GA treated group compared to diabetic and control groups. All testes of diabetic rats displayed obvious degeneration; whereas slight degeneration was seen in GA treated rats when compared to diabetic control group.

Conclusions: Our findings imply that GA may protect testis via enhancement of antioxidant capacity, it may be useful to meliorate the diabetic fertility complications.

1. Introduction

Natural substances have been used as a source of medicinal treatments for several decades [1,2], and plants-based products play a critical role in the treatment of diabetes mellitus (DM) globally [3]. In underdeveloped and developing countries worlds, herbal medicine is considered as a traditional medicine for treatment of diabetes [4]. The worldwide increased infertility or sterility rates have been a hotly debated problem [5], mainly on the comparative contributions of obesity and metabolic disorder factors [6,7]. Infertility is an important clinical problem, affecting people psychosocially [8] and medically [9]. In recent years, oxidative stress has been implicated in the progression of male infertility [10]. The experimental evidence has been implicated that these damages are caused by free radicals [11]. The deleterious effects of oxidative stress results

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from either an increased production of reactive oxygen species [12] or a decreased natural cell antioxidant capacity of an organism [13]. However, the utilization of foods rich in antioxidant phytochemicals may decrease the harmful effects caused by oxidative damage in several tissues including liver, intestine and kidney [14].

DM is a metabolic disorder characterized by high blood glucose levels due to the defects in the secretion of insulin and its action or both [15]. The chronic hyperglycemia is linked with protracted dysfunction, damage, and collapse of functioning of a variety of organs, including kidneys [16], nerves, heart [17], and blood vessels [18] and testis [19,20]. Hyperglycaemia generates reactive oxygen species [21], which sequentially cause cell damage via different pathways [22–24]. The damage of the cells ultimately results in the secondary complications of DM [25]. Numerous studies from the diabetic patients and experimental animals confirmed that sustained hyperglycemia resulted in the reduction of reproductive performance [26–28]. Since high blood glucose probably lead to the oxidative stress and cellular apoptosis [29,30], which in turn lead to the structural and functional impairments [27] and finally contribute to infertility [31,32]. Recent studies have broken the age factor in DM as it diagnosed both in younger and overage persons [33]. Therefore, diabetes-induced reproductive dysfunction is emerging as a new and urgent challenge [27]. The molecular mechanism through which diabetes induces male infertility is not fully understood.

Many experimental and clinical reports have been conducted on the molecular mechanisms responsible for the changes induced by DM in reproductive system of male but much remains to be clarified [34]. Some studies implicated that the diabetes induced male infertility through histological damage of the epididymis [28], decreased sperm motility [35], semen volume [36], sperm counts, motility and morphology [37] and disruption of seminiferous tubular morphology [38]. Moreover, DM induced male infertility via decreasing serum levels of luteinizing hormone, follicular stimulating [39] and testosterone [40].

Gum arabic (GA) is an edible, dried sticky exudate from *Acacia seyal* and *Acacia senegal*, which is rich in soluble dietary fiber. It is universally used in food manufacturing and pharmaceutical preparations as preservative and emulsifier [41]. In the Middle East and North Africa, it has been given orally as traditional medicine by different communities for centuries [42]. GA has been used to decrease both frequency and need of hemodialysis in patients who suffer with chronic renal failure [43]. It has powerful antioxidant properties, and used to decrease the experimental nephrotoxicity induced by gentamicin [43], cisplatin [44] and to decrease cardiotoxicity [45]. Moreover, GA is reported to reduce oxidative and inflammation against adenine induced chronic renal failure in rats [46] and improved the kidney functions in diabetic rat [47,48]. Yet, the effects of GA on oxidative stress in testis of type I diabetic rats have not been conducted. Moreover, it is less clear whether GA can alter oxidative related enzymes activity and genes expression in testis of type I a diabetic rat.

Therefore, in the current experiment, we used type I diabetic rat model to examine our assumption that the treatment of GA in the form of drinking water may decrease the oxidative damage in the testis, and the reduction of oxidative stress may associate with alteration of oxidative related genes expression in tests.

2. Materials and methods

2.1. Animals and experimental protocol

Male Sprague–Dawley rats 90 d of age, weighing (200 ± 10) g were purchased from Shanghai Laboratory Animal Center, Chinese Academy of Science and were housed under controlled environment with a 12 h light–dark cycle. The rats were adapted for one week prior to start the study and provided free access to water and standard rat rations throughout the experimental period. The rats were then divided into 3 groups: control group (n = 20) provided standard animal pellet and water *ad labitum*; diabetic group, intraperitoneal alloxan injected (n = 20); and diabetic group (n = 20) offered 15% GA in drinking water for 8 weeks. The GA was obtained from Sudanese Company for GA (Khartoum, Sudan). The dose of GA and the time duration was chosen based on our previous studies [49]. Type I DM was induced as described by Adeyi *et al.* [50]. Briefly, alloxan monohydrate was purchased from Sigma–Aldrich China (Shanghai, China), and type I DM was induced by single intraperitoneal injection of 150 mg/kg of alloxan monohydrate dissolved in normal saline after an overnight fast. Surviving rats after 3 d that have blood glucose levels more than 200 mg/dL were classified as type I diabetic models rat, were used for further study. All diabetic rats were euthanized after 8 weeks of treatment. The animals were fasted overnight, blood samples were collected prior to euthanasia. Body weights and organ weights were measured; blood and tissue samples were collected and kept at −80 °C for mRNA expression analysis.

2.2. Assessment of testis oxidative stress

Lipid peroxidation in testis was assessed by measuring the amount of malondialdehyde (MDA) as described by Bloom *et al.* [51] using obtainable commercial MDA kit (Nanjing Jiancheng Bioengineering Company, Nanjing, China). The MDA was measured in a UV spectrophotometry at 532 nm as described in the manufacturer's instructions. Approximately, 0.5 g of testis tissues were homogenized in 4.5 mL of ice-cold PBS buffer for preparation of testis homogenate, the homogenates were then centrifuged for 10 min at 3 000 r/pm and the supernatant was kept at −20 °C until analyzed. The levels of MDA in the tissue were expressed as nmol/g tissue.

Glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) kits were purchased from a commercial company (Nanjing Jiancheng Bioengineering Company, Nanjing, China). About 1 g of testis tissues were cut into small pieces then homogenized in ice-cold normal saline (0.85%, pH = 7.4) (1:9, wt/v) with an Ultra-Turrax (T8, IKA-labortechnik Staufen, Germany). Testis homogenates were centrifuged at 1 000 g for 15 min at 4 °C, and the supernatants were collected. The supernatants were used for the assays of SOD, GPx, CAT and GSH. SOD activity was measured as described by Cohen *et al.* [52]. The specific activity was

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