Inhibitory effect of fucoidan on hypoglycemia in diabetes mellitus anim

Xiao-Dong Yang, Cheng-Gong Liu, Yan-Juan Tian, Da-Hong Gao, Wan-Sen Li, Hai-Li Ma

Department of Integrated Internal Medicine, Zhumadian Central Hospital, Zhumadian, Henan, P. R. China

Abstract: In the present study effect of fucoidan on body weight, blood glucose, superoxide dismutase (SOD) and malondialdehyde (MDA) levels in streptozotocin (STZ) induced diabetes mellitus (DM) rat model was investigated. The animals were randomly assigned to four groups of 10 each: Normal group, diabetic group, diabetic group treated with 50 mg/kg and diabetic group treated with 100 mg/kg body weight fucoidan. For the preparation of DM rat model animals were fasted for 18 h and then injected with 60 mg/kg doses of STZ in citrate buffer. Induction of DM in the rats was confirmed by determining the blood sugar level in blood samples collected from tail vein of the rats. The results revealed that fucoidan treatment at a concentration of 100 mg/kg body weight caused a significant increase in the weight of animals compared diabetic group. Fucoidan treatment in rats reduced the blood sugar level which was increased by STZ administration in the diabetic group. Furthermore, fucoidan treatment promoted the activity of SOD, reduced the fasting blood glucose (FBG) level and inhibited the MDA level in the rats. Thus, fucoidan prevents DM in the STZ induced rat model through prevention of oxidative damage.

Keywords: Diabetes, fucoidan, oxidative damage, sugar, activity

Introduction

Fucoidan is the natural product possessing highly sulfated skeleton resembling structurally to the heparin and were isolated from the brown macro algae present in the sea [1]. The discovery of fucoidans is the result of efforts made in early nineteenth century by Kylin [2]. Later on, fucoidans were also isolated from a large number of weeds present in the British sea [3]. Analysis of the biological activity of fucoidan has revealed its role as a potent antithrombotic agent in vitro [4]. Fucoidan also acts as a strong antiproliferative agent against smooth muscle cells and heparin-resistant smooth muscle cells [5]. In addition, role of fucoidan as an inhibitor of kidney fibroblasts proliferation has also been identified [6].

Diabetes mellitus (DM) is a globally recognized health problem interlinked with various complications that worsen the quality of life and influence the survival of the affected people [7]. In various types of carcinomas like liver, breast and pancreas the major risk factor associated is the DM [8]. Investigation of the mechanism for understanding role of DM in cancer risk has led to believe that anti-apoptotic factors are activated by insulin and associated growth factors [9]. Studies have also revealed that DNA of the DM patients shows damage evidently caused by the oxidative processes [10]. Currently available drugs for maintaining blood sugar level in DM patients need to be taken regularly which induced side effects [11]. Thus the discovery of novel molecules and development of treatment strategies for DM is needed. Taking into consideration the need for development of new treatment strategies of DM several bioactive compounds including, sterols, terpenoids, flavonoids, and alkanooids have been screened [12]. In the present study role of fucoidan in the treatment of DM was investigated.

Materials and methods

Reagents

Fucoidan and streptozotocin were obtained from purchased from Sigma-Aldrich (St. Louis, MO, USA). Dimethyl sulfoxide (DMSO) and other common were obtained from the BD Pharmingen Inc. (San Diego, CA, USA). Kits for
the determination of glucose, superoxide dismutase (SOD) and malondialdehyde (MDA) were purchased from Invitrogen (Carlsbad, CA, USA).

Animals

8-week old male Sprague Dawley rats (180-200 g) were obtained from the Laboratory Animal Center of Sun Yat-sen University. The animals were housed in animal house facility of our institute under 12 h dark and light cycles at 22-25°C with 60-70% humidity and had free access to standard diet and water. The animals were randomly assigned to four groups of 10 each: Normal group, Diabetic group, Diabetic group treated with 50 mg/kg and Diabetic group treated with 100 mg/kg body weight fucoidan. All the experiments on animals were performed according to the guidelines of the National Institute of Health criteria for the care and use of laboratory animals. Approval for the present study was taken from the Laboratory Animal Care Committee of Sun Yat-sen University (Guangzhou, China).

Preparation of diabetes mellitus rat model

For the preparation of DM rat model animals were fasted for 18 h and then injected with 60 mg/kg doses of STZ in citrate buffer. Induction of DM in the rats was confirmed by determining the blood sugar level in blood samples collected from tail vein of the rats. The blood glucose level of the STZ injected rats rose to more than 11.0 mmol/L.

Treatment strategy

The animals in the two treatment groups were injected with 50 and 100 mg/kg body weight of fucoidan daily for one month. Rats in the normal and diabetic groups were given normal saline daily for one month at the same time. For each of the animal under study weight of the body and blood sugar level was measured weekly. After completion of the study, the animals were sacrificed to extract kidney, lungs, pancreas and liver. The extracted organs were separately washed and homogenized using Tris-HCl buffer. The supernatant from the liver homogenate was decanted and then used for the determination of SOD activity and measurement MDA level.

Statistical analysis

The data presented are the mean of ± SD. SPSS software, version 12.0 (SPSS, Inc., Chicago, IL, USA) was used for the analysis of the data. Differences between the groups were analyzed by one-way analysis of variance and Tukey post hoc comparisons. P<0.05 was considered to indicate a statistically significant difference.
Inhibitory effect of fucoidan on hypoglycemia in diabetes mellitus

Results

Fucoidan treatment resulted normal increase in the body weight of diabetic rats

Comparison of the body weights of the animals under study on day 10, 20 and 30 after induction of diabetes revealed a constant weight in diabetic rats but the body weight of the animals in the control group increased significantly (P>0.03) (Figure 1). Treatment of the diabetic rats with fucoidan prevented the diabetes mediated inhibition of increase in the body weight. Body weight of the animals in the 100 µM treatment group showed similar increase to that of the normal group. However, increase in the body weight of animals in 50 µM treatment group was lower compared to the 100 µM treatment (P<0.03).

Fucoidan treatment inhibited increase in the fastening blood glucose (FBG) levels

In the diabetic rats level of FBG was increased significantly compared to normal group. However, fucoidan treatment exhibited inhibi-
Inhibitory effect of fucoidan on hypoglycemia in diabetes mellitus

Fucoidan treatment enhanced activity of SOD

In the diabetic group of rats, activity of SOD was decreased significantly compared to normal group (P<0.03). Treatment of the diabetic rats with fucoidan promoted the activity of SOD and the activity was similar among the animals in normal control and 100 µM fucoidan treatment groups. However, SOD activity in the animals of 50 µM fucoidan treatment group was lower than those in the 100 µM treatment group (Figure 4A).

Fucoidan treatment inhibited increase in the MDA level in diabetic rats

Fucoidan exhibited inhibitory effect on the level of MDA production in various tissues of the rats compared to the control group. Reduction in the level of MDA by fucoidan was concentration dependent. In the untreated group, MDA level was significantly (P<0.02) higher compared to the rats treated with 100 µM doses of fucoidan. The rats in the 50 µM fucoidan treatment group showed higher level of MDA than those in the 100 µM treatment group (Figure 4B). MDA level was similar in the rats of 100 µM fucoidan treatment and the normal groups.

Discussion

Fucoidan resembles heparin structurally and is a sulfated glycosaminoglycan which exhibits antithrombotic effects in vitro [1, 3]. Fucoidan has been shown to act as a potent anti-proliferative agent against smooth muscle cells and heparin-resistant SMCs [4, 5]. Present study demonstrates the role of fucoidan in the treatment of STZ induced diabetes mellitus in the rat model. DM causes a marked reduction in the body weight of the animals because of the decrease in FBG level. The decrease in FBG level was significant at 100 µM doses of fucoidan from day 5 of the treatment (Figure 2).

Examination of the level of glucose in blood following 20, 40, 80 and 120 min revealed significant increase in the diabetic group of rats compared to the normal group. However, treatment of the rats with fucoidan inhibited the increase in the level of blood glucose. The inhibition of increased blood glucose level was significant in 100 µM fucoidan treatment group compared to the 50 µM treatment group (P<0.03) (Figure 3).

**Figure 4.** Fucoidan treatment (A) promoted STZ induced inhibition in superoxide dismutase (SOD) activity and (B) reduced MDA level which was increased by STZ in the rats. The data expressed are the means ± SD. Compared to the control group P<0.03.
degeneration of proteins associated with structural framework [13].

In many studies it has been observed that body weight of the diabetic animals continues to decrease during study period. Results from the present study demonstrated that fucoidan treatment inhibited the STZ induced reduction in the body weight. Animals in the fucoidan treatment group showed increase in the body weight similar to those of the normal rats. In the patients with DM, blood glucose increases significantly which then worsens the health and induces several side effects [14, 15]. Our results revealed significant increase in the blood glucose in STZ induced diabetic rats consistent with the earlier reports. However, fucoidan treatment inhibited STZ induced increase in the blood sugar level and maintained it constant in the rats. DM has been found to be associated with the production of large quantity of oxidative species and suppression in the formation of radical scavenging agents because of the intervention of sugar molecules [16, 17]. Results from the present study revealed that fucoidan treatment in the STZ-induced diabetic rats promoted the activity of SOD significantly. In addition, the level of MDA was reduced significantly compared to the untreated rats.

In conclusion, current study demonstrates that fucoidan treatment exhibits protective effect against STZ induced reduction in body weight, increase in blood sugar, reduction in SOD activity and increase in MDA level in the rats. Therefore, fucoidan has a scope for being evaluated further against DM.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Cheng-Gong Liu, Department of Integrated Internal Medicine, Zhuminian Central Hospital, 747 Zhonghua Road, Nanching District, Zhumadian 463000, Henan, P. R. China. Tel: 0086-396-2726999; Fax: 0086-396-2726999; E-mail: chenggongir@hotmail.com

References

Inhibitory effect of fucoidan on hypoglycemia in diabetes mellitus


