

The Effects of Myo-inositol on Glucose Metabolic in Diabetes Rats

Yin Xue-ping^{1,2}, Guo Fei-fei¹, Sun Xiangrong¹, Xu Luo¹ 

¹Dept. of Pathophysiology, Medical College of Qingdao University, Qingdao, Shandong, 266021, China

²Gaomi City People's Hospital, Gaomi, Shandong, 261500, China

Abstract: Objective: To observe the myo-inositol on normal and diabetic rats muscle and intestinal glucose uptake. **Methods:** The rat jejunum was placed in Kb with containing 2.5% -20% myo-inositol and the glucose concentration was detected at 0 and 2 h. The psoas muscle was placed in Kb containing 2.5% -20% myo-inositol Kb (with or without insulin) the glucose concentration was detected at 0 and 1 h. Rats were divided into blank control group, normal muscle myo-inositol group, blank control group of diabetic rats, myo-inositol group of diabetic rats and acarbose group of diabetic rats (DBA) The intestinal propulsion rate and intestinal absorption of glucose in each group were detected. **Results:** In vitro studies found that myo-inositol can dose-dependently stimulate the absorption of glucose in the jejunum and promote the uptake of glucose by the psoas muscle in a dose-dependent manner. Myo-inositol can delay gastric emptying in diabetic rats, inhibit intestinal absorption of glucose, reduce postprandial blood glucose in diabetic rats and promote the rate of intestinal propulsion in diabetic rats. **Conclusion:** Myo-inositol can inhibit the intestinal absorption of glucose in glucose rats and promote the glucose uptake in muscle of normal rats and diabetic rats.

Keywords: Inositol, Diabetes, Glucose Metabolic

Introduction

There are two major types of diabetes type I and II, of which type 2 diabetes (T2D) is the most common type of diabetes, accounting for more than 90% of all cases of diabetes^[1]. Sedentary, high-fat and high-sugar diets, and high intakes of refined sugars and monosaccharides keep the body in high blood sugar for a long time^[2]. For the treatment of diabetes, in addition to conventional antidiabetic drug therapy to reduce high-calorie and high-sugar food intake, and the combination of drugs inhibiting an increase in blood sugar after a meal has become more comprehensive diabetes treatment programs^[3].

Myo-inositol, a less used sugar alcohol, is similar in structure to glucose and is found in a variety of foods, but at lower concentrations^[4]. D-inositol is another high content of inositol in fat, muscle and liver^[5]. Myo-inositol with glucose transporter activation and glucose utilization, D-inositol is mainly involved in the synthesis of glycogen in liver, fat and muscle tissue^[4]. Studies have also found that supplementation with myo-inositol can regulate glucose and lipid metabolism, the glucose and lipid metabolism are closely related to the pathogenesis of T2D.^[6]

At present, it is not yet clear whether muscle myo-inositol can affect glucose uptake by muscles, nor does research clearly indicate that myo-inositol can affect intestinal absorption of glucose. Therefore, this study investigated the effects of muscle inositol on glucose and glucose absorption in muscle and intestine of normal and diabetic rats through in vitro and in vivo studies.

1 Materials and Methods

2 Animals

7-week-old male Sprague-Dawley rats were 184.20±5.22 g, room temperature was controlled at 25±2°C, and day and night cycling light was used for 12 h, and the diet was free. All animals followed the "Qingdao University Laboratory Animal Protection and Use Management Methods." All experiments were in accordance with the Qingdao Experimental Animal Center.

1.2 In vitro studies

5 rats were randomly selected and sacrificed after fasting for 12 h. The entire gastrointestinal tract (GIT) and psoas muscles were dissected and used for glucose absorption and uptake studies.

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Xu Luo (Correspondence)



xuluo1234 @ 126.com



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1.2.1 Absorption of glucose by jejunum

5 jejunum of 5 cm in length were randomly selected from the gastrointestinal tract of each rat and placed in 8 ml of Kb fluid (118 mM NaCl, 5 mM KCl, 1.328 mM $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, 1.2 mM KH_2PO_4 , 1.2 mM MgSO_4 and 25 mM NaHCO_3) was filled with a mixture of 5% CO_2 and 95% O_2 , each containing 11.1 mM (199.98 mg/dL) Glucose was placed at a constant temperature of 37°C.

1.2.2 Absorption of glucose by psoas muscle

12 rat psoas muscles were weighed at random, each 0.5 g, divided into insulin (200 mU/mL) group and no insulin group (n=6), each component was muscle myo-inositol (2.5%, 5%, 10%, 20%), metformin (2 mg/mL) and placebo, each psoas muscle was placed in 8 ml Kb solution containing 11.1 mM (199.98 mg/dL) glucose, filled with 5% CO_2 and A mixture of 95% O_2 , insulin solution containing 200 mU/mL insulin in the Kb solution, each group were placed at 37 °C constant temperature experiments, and before the test and 1 h after the start of the test kit to detect Kb The concentration of glucose in the liquid.

1.3 In vivo studies

1.3.1 Diabetic rat model preparation

Diabetic rats were given 10% fructose solution to induce insulin resistance in rats, and normal rats were given normal drinking water. 40 mg/kg streptozotocin was injected intraperitoneally into diabetic rats, whereas in normal rats, citrate buffer was only injected intraperitoneally. One week after intraperitoneal injection, the rats' postprandial blood glucose was measured. Rats with postprandial blood glucose >300 mg/dl were selected as diabetic rats for study.

1.3.2 Rat grouping

12 normal rats were randomly selected and divided into 2 groups (n=6), normal rats blank control group (NC), and normal rat muscle myo-inositol group (NMI). 18 diabetic rats were randomly selected and divided into 3 groups (n=6), diabetic control group (DBC), diabetic myo-inositol group (DMI), diabetic rat acarbose group (DBA).

The fasting blood glucose was measured after overnight fasting in rats. Rats in NMI and DMI groups

were orally administered with a mixture of myo-inositol (1 g/kg) and glucose (2 g/kg). DBA rats were gavaged the mixture of acarbose (100 mg/Kg) and glucose (2 g/kg). The rats in the NC and DBC groups were gavaged glucose (2 g/kg). 0.05% phenol red was present in all gavage fluids. All rats were anesthetized with sevoflurane for 1 h after gavage, blood samples were collected by cardiac puncture, and the rat gastrointestinal tract (GIT) was isolated. The kit was used to detect the glucose level in the blood samples of the rats. The GIT was quickly frozen in liquid nitrogen and retained at -30°C.

1.3.3 Intestine advancing rate and intestinal glucose absorption

The GIT was divided into 8 segments. The stomach and small intestine were divided into 4 segments. The cecum and the colon were divided into 2 segments. After each segment was weighed, the contents of each segment were measured by the kit to measure the glucose concentration, and each segment of the content and tissue was separated. After homogenization, 15000 rpm centrifuged for 30 min. The supernatant was used to measure the absorbance at 620 nm. The phenol red concentration in each gastrointestinal tract was determined by referring to the phenol red standard absorbance luminosity curve. Calculate the gastric emptying rate (%), the intestinal propulsion rate (%), and the glucose absorption index (GAI).

1.4 Statistical analysis

The data in the experiment was represented by $\bar{X} \pm \text{SEM}$. The data was statistically analyzed using Prism 5.0. T-test or one-way ANOVA was used between the two groups. $P < 0.05$ was considered statistically significant.

2 Result

2.1 In vitro studies

2.1.1 Effect of Myo-Inositol on Absorption of Glucose in the Jejunum of Isolated Rats

In vitro studies found that myo-inositol inhibited glucose uptake in the jejunum of rats in a dose-dependent manner ($p < 0.05 \sim 0.001$). Myo-inositol at a concentration of 10% achieved a maximum inhibitory effect.

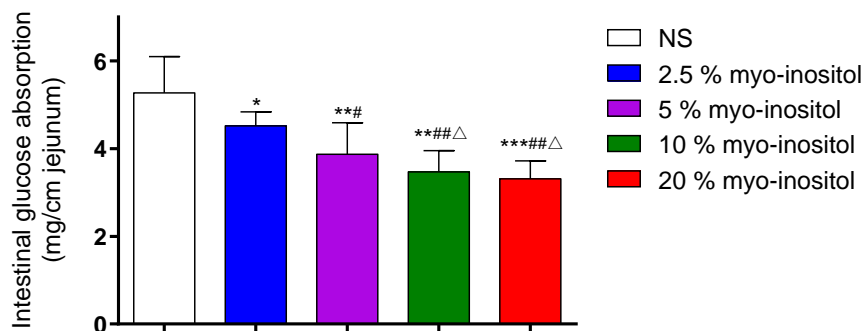


Fig.1 Effect of Muscle Inositol on Absorption of Glucose in Jejunum of Rats

*p<0.05, **p<0.01, ***p<0.001, vs. NS group; #p<0.05, ##p<0.01 vs. 2.5% myo-inositol group; Δp<0.05 vs. 5% myo-inositol group

2.1.2 Effect of Myo-Inositol on Glucose Uptake in Rat Psoas Muscle

In vitro studies have shown that myo-inositol promotes glucose uptake in the psoas muscle in a dose-dependent

manner (p<0.05~0.001). This effect of myo-inositol promotes muscle uptake of glucose can be enhanced by insulin (p<0.05).

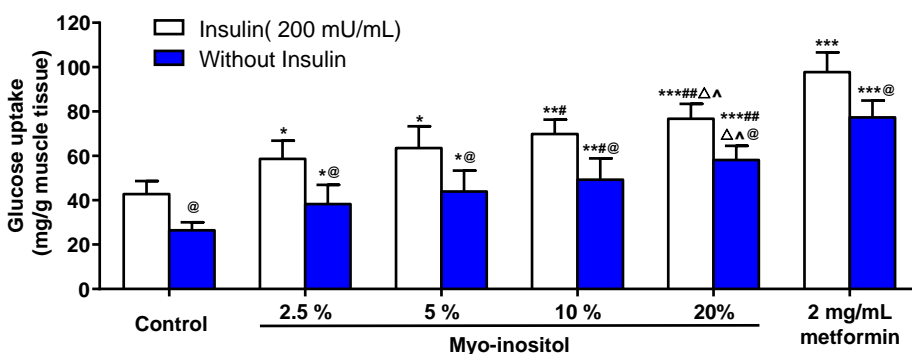


Fig. 2 Effect of Muscle Inositol on Glucose Uptake in Rat Psoas Muscle

*p<0.05, **p<0.01, ***p<0.001 vs. the control group with same insulin concentration; #p<0.05, ##p<0.01 vs. 2.5% myo-inositol with same insulin concentration; Δp<0.05 vs. 5% myo-inositol with same insulin concentration; ^p<0.05 vs. 10% myo-inositol with same insulin concentration

2.2 In vivo studies

2.2.1 Effect of Myo-Inositol on Gastric Emptying

Compared with diabetic rats given physiological saline, gastric emptying was decreased in diabetic with

myo-inositol and acarbose rats (P<0.05), but there was no significant change in gastric emptying after administration of myo-inositol in normal rats.

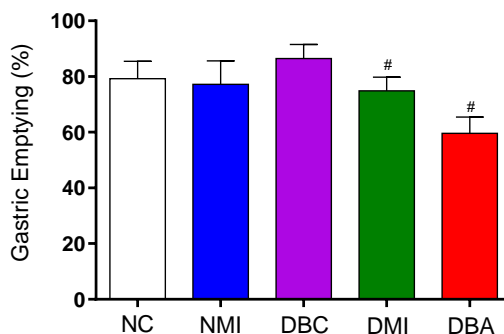


Fig. 3 Effect of Myo-Inositol on Gastric Emptying

#p<0.05 vs. DBC group; ^p<0.05 vs. DMI group

2.2.2 Effect of myo-inositol on intestinal absorption of glucose

In vivo studies found that myo-inositol can reduce glucose absorption in the first and second segments of the small intestine in normal rats ($p < 0.05$), and in

diabetic rats, glucose uptake in the first small intestine and cecum of diabetic rats after administration of myo-inositol ($p < 0.05$). Acarbose inhibits glucose uptake in the first segment of the small intestine and the first segment of the colon in diabetic rats ($p < 0.05$).

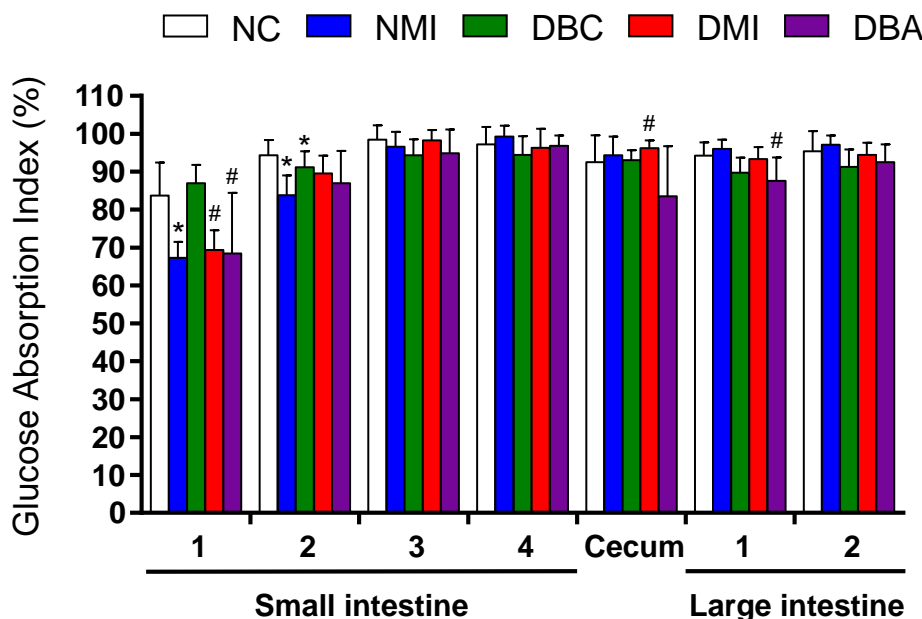


Fig. 4 Effect of myo-inositol on intestinal absorption of glucose
* $p < 0.05$ vs. NC group; # $p < 0.05$ vs. DBC group

2.2.3 Effect of Myo-Inositol on Blood Glucose

Myo-Inositol can not reduce blood glucose in normal rats 1 h after meal, but it can reduce the blood glucose

level 1 hour after meal in diabetic rats. ($p < 0.05$), Acarbose reduces blood glucose 1 h after meal in diabetic rats ($p < 0.05$).

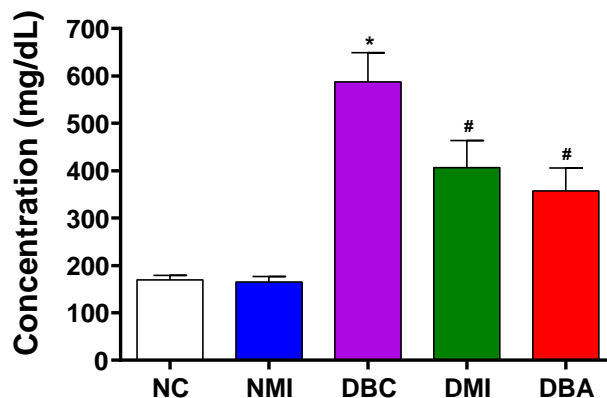


Fig. 5 Effect of Myo-Inositol on Blood Glucose
* $p < 0.05$ vs. NC group; # $p < 0.05$ vs. DBC group

2.2.4 Effect of Myo-Inositol on Intestinal Propulsive Rate

Myo-inositol improves intestinal propagation rates in the third, fourth, cecum and colon of normal and

diabetic rats ($P < 0.05$), and acarbose can only promote the intestinal propulsion rate of the first small intestine, cecum and colon in diabetic rats ($P < 0.05$).

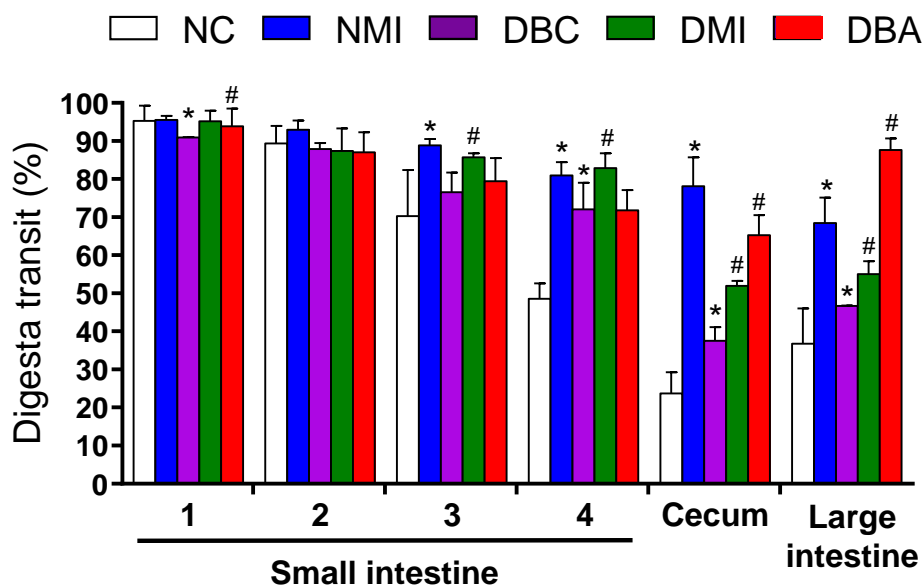


Fig. 6 Effect of myo-inositol on intestinal propulsive rate
* $p < 0.05$ vs. NC group; # $p < 0.05$ vs. DBC group

3 Discuss

Insulin enhances glucose metabolism to ensure stable blood sugar [7]. In patients with type 2 diabetes, insulin resistance or down-regulation of insulin sensitivity results in decreased glucose uptake by myocytes, lowering glucose tolerance in the body, and resulting in persistent hyperglycemia. [8].

Since the uptake of glucose by muscle cells is an important indicator of insulin sensitivity, the effect of myo-inositol on glucose uptake in isolated rat psoas muscle (with or without insulin) was investigated in our study to investigate whether myo-inositol can improve the insulin sensitivity of diabetic patients. In this study, it was found that myo-inositol promoted the glucose uptake of isolated psoas muscle (with or without insulin) in a dose-dependent manner. It has been shown that at least in vitro, myo-inositol enhances glucose uptake by insulin-mediated muscles, but this finding is only ex vivo muscle and does not represent muscle regulation of glucose uptake in vivo. Supplementing myo-inositol may improve insulin sensitivity in somatic skeletal muscle [5,6].

For glucose uptake, different segments of the small intestine have different glucose uptake [9], therefore, we mainly observed the absorption of glucose in this part of the intestine during the study. In vitro studies found that myo-inositol inhibits the absorption of glucose in the intestine in a dose-dependent manner, indicating that myo-inositol has the potential to reduce postprandial blood glucose. In vivo study also found that normal rats, diabetic rats after the administration of

myo-inositol in the first segment of the small intestine to glucose uptake, and to diabetic myo-inositol diabetic rats postprandial blood glucose increased significantly lower than Diabetic rats that were not given muscle myo-inositol. It was shown that myo-inositol may have the potential to inhibit the intestinal uptake of glucose in food.

Reduced gastric emptying and increased intestinal propulsion can reduce nutrient absorption and food intake in the intestine [10], our study found that gastric emptying in diabetic rats increased, which is similar to the clinical manifestations of most patients with type 2 diabetes [11]. This study found that gastric emptying in diabetic rats after intramuscular administration of myo-inositol was delayed, and both normal and diabetic rats showed an increase in the intestinal propulsion rate of the eel, which may be due to the similar structure of myo-inositol and glucose. It is able to competitively inhibit glucose, but this still needs further research to confirm.

Taken together, this study found that myo-inositol inhibits the absorption of glucose by the jejunum and increases glucose uptake by isolated muscles in vitro. Oral myo-inositol inhibits the absorption of glucose in the proximal small intestine and inhibits it. Gastric emptying increases the bowel intestine advancing rate. Although the results of this study found that oral myo-inositol can reduce postprandial blood glucose in diabetic rats, it is not entirely certain that this is due to myo-inositol inhibiting glucose absorption in the proximal small intestine. However, the results of the

current study show that diabetic patients given a certain amount of myo-inositol can help control postprandial blood glucose, reduce intestinal glucose absorption, increase muscle glucose uptake, which will provide new drugs for clinical diabetes patients direction.

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