The effect of troxerutin on alterations of lipid profile and biochemical enzymes in blood of rats with chronic diabetes

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A b s t r a c t

Diabetes Mellitus (DM) is a progressive disease that leads to complex disorders such as biochemical changes in the blood. The use of medicinal plants are superior to synthetic drugs because of the few side-effects in disease prevention. In this study, we examined the effect of troxerutin on lipid profile and biochemical enzymes in the blood of type 1 diabetic rats. 32 male Wistar rats (200-250) were randomly divided into four groups: control, diabetes, control+ troxerutin, diabetes+ troxerutin. Type 1 diabetes was induced by i.p injection of streptozotocin (50 mg/kg) in animals in diabetic groups. Lasted for 4 weeks, oral administration of troxerutin (150 mg/kg) was carried daily for 4 weeks. At the end of study, anesthesia was induced intraperitoneally with sodium pentobarbital (mg / kg 60). Blood samples was collected for measuring lipid profile and biochemical enzymes in blood of rats. Diabete significantly increased LDL, COL, TG and significantly decreased HDL compared to the control group. Treatment diabetic rats with troxerutin for 4 weeks significantly decreased LDL, COL, TG and significantly increased HDL. Furthermore, Diabetes significantly increased ALT, AST, LDH, and CPK in blood of rats. Treatment diabetic rats with troxerutin for 4 weeks significantly decreased ALT, AST, LDH, and CPK in blood of rats compared to the control group. Troxerutin improve the lipid profile and reduce biochemical enzymes in blood of diabetic rats. In this way could be useful in reducing the complications of diabetes.

Keywords: Diabetes, Troxerutin, biochemical enzymes, lipid profile, rat.

Introduction

Diabetes mellitus (DM) is a syndrome characterized by disordered metabolism, hyperglycemia, resulting from low levels of insulin production by beta cells of pancreas [1]. Approximately 95% of diabetics are suffering from dyslipidemia and have changes in their total blood protein [2]. Blood levels of liver enzymes in diabetic subjects are changed compared with healthy subjects (non-diabetic) [3]. Prospective studies have found that high levels of hepatic enzymes, including alanine amino transferase (ALT), aspartate transferase (AST) and alkaline phosphatase (ALP) are associated with later development diabetes [4]. It is reported that increased levels of ALT is precursor to type 2 diabetes [4]. Also, elevation of serum lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) concentration has been observed in patients with diabetes mellitus [5]. Hypoglycemic agents are useful in the treatment of DM, but have many side effects and use of these drugs restricted by the pharmacokinetic properties and secondary failure rates. So, there is a need to look for more efficacious agents with fewer side effects[6]. Troxerutin, a trihydroxyethylated derivative of the natural bioflavonoid rutin, has been reported to possess important biological activity, including antioxidative, anti-inflammatory, anti-hyperlipidemia and anti-thrombolytic activity [7]. It is shown that troxerutin decrease advanced glycation end products and oxidative stress in mice. Many studies have shown that troxerutin has a variety of biological activities [8-11]. Therefore, due to the possible effects of troxerutin in control of diabetes, this study is designed to investigate the effects of troxerutin on alterations of lipid profile and biochemical enzymes in blood of rats with chronic diabetes.

Methods

Animals and study design

This research was carried out in accordance with the National Research Council’s protocol for the care and use of laboratory animals. We obtained 32 Wistar male rats (200 to 250 g) from the laboratory animal house of Tabriz University of Medical Sciences. The animals were housed in standard conditions (temperature 22 C, light from 8.00 am to 8.00 pm) and had free access to tap...
water and food pellets. The animals were divided into four groups (n = 7):
1- Control (Con): animals that have no intervention and received placebo for 4 weeks.
2- Diabetes (Dia): animals that were diabetic and received placebo for 4 weeks.
3- Troxerutin (Trx): animals that received troxerutin (150 mg/kg/day) for 4 weeks.
4- Diabetes + troxerutin (Dia-Trx): diabetic rats that received troxerutin for 4 weeks.

Troxerutin (150 mg/kg) was gavaged 6 days a week for 4 weeks.

Biochemistry Analysis

At the end of the treatment period of 4 weeks, the animals were sacrificed after overnight fasting and blood for serum was collected. The blood collected without EDTA was centrifuged at 3500 rpm during 15 minutes to obtain the serum that was stored at -20ºC. The serum concentration of liver enzymes (alanine aminotransferase - ALT, aspartate aminotransferase - AST, and alkaline phosphatase - ALP) were determined by colorimetric assay using commercially available kits according to the manufacturer’s instructions (Labtest Diagnóstica S.A., Lagoa Santa, MG, Brazil). Biochemical parameters including total cholesterol (TC), triglycerides (TGs), high density lipoprotein-cholesterol (HDLc), and low density lipoproteincholesterol (LDLc) that were determined enzymatically on a COBAS FARA analyzer Roche Diagnostics, Switzerland [14].

Statistical analysis

All values were analyzed by one-way analysis of variance (ANOVA), and the Tukey test was used to compare quantitative data. Values less than 0.05 were considered statistically significant in all cases. Results are expressed as means ±SEM.

<table>
<thead>
<tr>
<th>متغيرها</th>
<th>Triglyceride (mg/dl)</th>
<th>Colesterol (mg/dl)</th>
<th>LDL (mg/dl)</th>
<th>HDL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Con</td>
<td>82/2 ± 10/2</td>
<td>65 ± 2/5</td>
<td>5/5 ± %2</td>
<td>%30 ± %2</td>
</tr>
<tr>
<td>Dia</td>
<td>100 ± 1/18**</td>
<td>105 ± 2/5 **</td>
<td>7/5 ± 0/6 **</td>
<td>%24 ± 0/07***</td>
</tr>
<tr>
<td>Con-Trx</td>
<td>75 ± 9/5 *</td>
<td>6 ± 5/5 ***</td>
<td>4/2 ± %78 ***</td>
<td>%38 ± %05 ***</td>
</tr>
<tr>
<td>Dia-Trx</td>
<td>91 ± 5/6*+++/**</td>
<td>78 ± 3/6 *<strong>+++/</strong></td>
<td>6/6 ±%10 <em>+/</em>+</td>
<td>%29 ± %05 ***</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SEM for 7 animals. * p<0.05, ** p<0.01, *** p<0.001 vs the Con group. + p<0.05, ++ p<0.01, +++ p<0.001 vs the Dia group. ## p<0.01, ### p<0.001 vs the Con-Trx group.

LDL: Low density lipoprotein - HDL: High density lipoprotein.
Con: Control, Dia: Diabetes, Con-Trx:Control-Troxerutin, Dia-Trx: Diabetes- Troxerutin.

Result

Effects of troxerutin on lipid profile (TG, COL, LDL, and HDL)

Tabel 1 shows that diabetes significantly (p< 0/01) increase TG, COL, LDL and significantly (p< 0/01) decrease HDL in blood in comparison to the control group. After 4 weeks of treatment of diabetic rats with troxerutin, the level of TG (p< 0.001), COL (p< 0/001), LDL (p< 0.01) and HDL (p< 0/05) significantly reversed in blood in comparison to the diabetes group. Also, in the Trx group, TG (p< 0/05), LDL (p< 0/01) significantly decreased and HDL (p< 0/01) significantly increased in blood in comparison to the control group.
Figure 1. A) Effect of 4 weeks troxerutine treatment on AST levels in the serum of the control and diabetes groups B) Effect of 4 weeks troxerutine treatment on ALP levels in the serum of the control and diabetes groups C) Effects of 4 weeks troxerutine on ALT levels in the serum of the control and diabetes groups D) Effects of 4 weeks troxerutine on LDH levels in the serum of the control and diabetes groups. Data are expressed as mean ± SEM for 7 animals. *p<0.05, ** p<0.001 vs the Con group. ++ p<0.01 , +++ p<0.001 vs the Dia group.

Effects of troxerutin on blood biochemical enzymes (ALT, AST, ALP, CKP, LDH)

One-way ANOVA showed that diabetes significantly(p<0/01) increase AST in blood in comparison to the control group. After 4 weeks of treatment of diabetic rats with troxerutin significantly (p<0/01) decrease AST in blood in comparison to the diabetes group. As shown in figure b, diabetes significantly (p<0/001) increase ALP in blood of Dia group in comparison to the control group. Treatment of diabetic rats with troxerutin significantly (p<0/01) decrease this enzyme. One way ANOVA in figure C shows that diabetes significantly (p<0/001) increase ALT in blood in comparison to the control group. Also, treatment with troxerutin significantly decrease ALT in control group (p<0/05) and diabetic rats (p<0/001). As shown in figure d, diabetes significantly (p<0/01) increase LDH in blood of diabetes group in comparison to the control group. Also, treatment of diabetic rats with troxerutin significantly decrease LDH in blood in comparison to the control group (p<0/05) and diabetes group (p<0/01).

Discussion

This study is the first to investigate the effect of troxerutin on lipid profile and biochemical enzymes in blood of rats with type 1 diabetes. In this study we shown that 4 weeks treatment of diabetes and control groups with troxerutin significantly decrease triglyceride, cholesterol, LDL and increase HDL in blood in comparison to the control group and diabetes group, respectively. Also, our findings showed that treatment of diabetic rats with troxerutin significantly decrease blood of biochemical enzymes in comparison to control group. Diabetes mellitus is associated with a cluster of interrelated plasma lipid and lipoprotein abnormalities, including reduced HDL cholesterol, a predominance of small dense LDL particles, and
References


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