



## **Beneficial Effect of Quercetin on Some Haematological Parameters in Streptozotocin-Induced Diabetic Rats**

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### **ABSTRACT**

*The aim of the study was to evaluate the beneficial and preventive effects of quercetin on some hematological parameters in streptozotocin (STZ)-induced diabetic rats. Experimental animals were divided into four equal groups as Control (C), Diabetes (D), Quercetin (Q) and Diabetes+Quercetin (DQ). STZ was injected at a single dose of 60 mg/kg (i.p) for diabetes induction. Quercetin (15 mg/kg) was injected (i.p) to the Q and DQ groups (after diabetes had happened) during 4 week. In blood samples, leukocyte (WBC), erythrocyte (RBC), hemoglobin (HGB), hematocrit (HCT), platelet (PLT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and differential leucocyte count were examined. In the study RBC and platelet counts, Hb and Htc levels in diabetic rats significantly decreased compared with control (C) and quercetin (Q) groups. These parameters were tending to increase in DQ group compared with D group. MCV, MCH, MCHC levels did not show any important changes in all groups. Leucocytes count was increased with diabetes and decreased obviously with quercetin treatment. Neutrophil count was increased in diabetic rats. On the other hand lymphocyte count was decreased in D group. And there were no significantly differences neutrophil and lymphocyte count with quercetin treatment in DQ group. In conclusion our results showed that further studies are needed about quercetin and its effects on diabetes with different amount and duration.*

**Keywords:** Diabetes Mellitus, Quercetin, haematological parameters, streptozotocin.

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### **INTRODUCTION**

Diabetes Mellitus (DM) is a complex and common metabolic disease involved multiple organs disorders. Its characteristics marker is high blood glucose level, leading to morbidity and mortality in worldwide. T1DM is caused by lack of insulin producing cells in pancreas, whereas there are insulin receptor resistances in T2DM. Both T1 and T2 DM can lead to serious chronic complications, such as cardiovascular disease, neural, renal and retinal disorders [3,5,14].

Some studies reported that oxidative damage played an important role in the pathogenesis of DM[16]. Further there are biochemical changes include mediation of vascular inflammation, autoimmune response activation and blood cell abnormalities in T1 and T2 DM[2].

Current pharmacological treatments of DM are established on hypoglycemic drugs and conventional insulin therapy [6]. Hence there are new therapeutic approaches in treatment of diabetes. In recent years studies has focused on alternative herbal medicine [5,23]. One of these alternative therapeutic agents is flavonoids. Quercetin as a flavonoid reported to prevent oxidant injury, cell death by assorted mechanisms. These mechanisms were stated as scavenging of oxygen radicals, protection from lipid peroxidation and chelation of metal ions [8].

In this study, it was aimed to determine the effects of quercetin on some hematological parameters in diabetic rats induced experimentally with streptozotocin (STZ).

### **Material and Methods**

#### *Experimental design and laboratory animals*

In the present study, 32 adult male Wistar albino rats were used. The research project and animal housing conditions were approved by the Ethical Committee for Animal Studies (2014-042). Rats were obtained from the Laboratory Animal Breeding Unit of Necmettin Erbakan University. Experimental

animals were divided into four equal groups as Control (C), Diabetes (D), Quercetin (Q) and Diabetes+Quercetin (DQ). The weights of groups were close to each other. STZ (60 mg/kg, live weight (Sigma S0130-1G)) were injected intraperitoneal to the D and DQ groups as a single dose. Quercetin (15 mg/kg, live weight/day) (Sigma Q4951) were injected intraperitoneal to the Q and DQ groups (after diabetes had happened) during 4 week. STZ and quercetin prepared freshly before the application.

60 mg/kg of STZ (Sigma S0130-1G) dissolved in 0.1 M citrate buffer (pH: 4.5) before used. After 72 hours STZ injection blood glucose levels was measured from the tail by blood glucose meters (plusMED). At the end of the 4 week trial period, blood samples were taken under anesthesia and collected by cardiac puncture, and transferred into anticoagulant tubes for determination.

#### Hematological Analyses

In blood samples, leukocyte (WBC), erythrocyte (RBC), hemoglobin (HGB), hematocrit (HCT), platelet (PLT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and differential leucocyte count were examined. Hematological characteristics were obtained using a cell counter (Mindray BC800).

#### Statistical analysis

Statistical differences among the groups were tested by analysis of variance (ANOVA) which is followed by Duncan's test using SPSS for windows version 16.0. Significant was considered as  $P < 0.05$ .

## RESULTS AND DISCUSSION

In the study RBC counts in diabetic rats significantly decreased compared with control (C) and quercetin (Q) groups ( $P < 0.05$ ), and RBC counts in DQ group were tending to increase insignificantly to D group. Hemoglobin and hematocrit levels of diabetic rats decreased with STZ treatment to control groups. Hb levels were found to be higher in DQ group than D group. Htc levels in DQ group dramatically increased compared to D group. Platelet counts in diabetic groups was significantly ( $P < 0.05$ ) lower that of control group, while there was no differences within D and DQ groups. Leucocytes counts were increased with diabetes and decreased obviously with quercetin treatment. On the other hand MCV, MCH, MCHC levels did not show any important changes in all groups. (Table 1).

Table1. Some hematological parameters in experimental groups,  $X \pm SX$

Parameters	C	Q	D	DQ
WBC( $\times 10^3/\text{mm}^3$ )	4.48 $\pm$ 0.43b	4.40 $\pm$ 0.72b	8.61 $\pm$ 1.14a	6.51 $\pm$ 0.36ab
RBC ( $\times 10^6/\text{mm}^3$ )	8.19 $\pm$ 0.17a	7.34 $\pm$ 0.55ab	5.69 $\pm$ 0.91b	6.87 $\pm$ 0.31ab
Hb (gr/dl)	14.93 $\pm$ 0.27a	13.50 $\pm$ 0.97ab	10.42 $\pm$ 1.85b	13.91 $\pm$ 0.59a
Htc (%)	48.75 $\pm$ 1.32a	46.81 $\pm$ 2.61a	32.93 $\pm$ 6.79b	42.60 $\pm$ 4.79ab
Plt (L)	763.16 $\pm$ 80.70a	854.50 $\pm$ 86.61a	412.0 $\pm$ 55.34b	500.66 $\pm$ 98.42b
MCV ( $\mu^3$ )	59.52 $\pm$ 1.54	66.86 $\pm$ 8.88	55.87 $\pm$ 5.01	62.44 $\pm$ 7.52
MCH (pg)	18,26 $\pm$ 0.33	18.39 $\pm$ 0.24	18.03 $\pm$ 0.35	20.31 $\pm$ 0.69
MCHC (%)	30.66 $\pm$ 0.34	29.75 $\pm$ 3.49	32.62 $\pm$ 5.21	35.46 $\pm$ 5.35

a, b;  $P < 0,05$

Table 2. Differential leucocyte counts (%) in experimental groups,  $X \pm SX$

%	C	Q	D	DQ
Lymphocyte	67.25 $\pm$ 5.41a	58.09 $\pm$ 6.93ab	49.65 $\pm$ 5.41b	55.50 $\pm$ 4.05ab
Monocyte	3.17 $\pm$ 1.17	3.91 $\pm$ 1.19	4.16 $\pm$ 0.88	4.19 $\pm$ 0.95
Neutrophile	26.85 $\pm$ 4.21b	35.48 $\pm$ 6.10ab	43.61 $\pm$ 4.20a	37.45 $\pm$ 2.82ab
Eosinophile	1.15 $\pm$ 0.46	1.35 $\pm$ 0.54	1.14 $\pm$ 0.57	1.22 $\pm$ 0.55
Basophile	1.58 $\pm$ 0.39	1.17 $\pm$ 0.27	1.42 $\pm$ 0.31	1.64 $\pm$ 0.39

a, b;  $P < 0,05$

The observed decreases in RBC, Hb, and Htc levels after induced Diabetes Mellitus are expected changes. It is well known that anemia occurred in chronic diseases[17, 22]. The developing of anemia in DM has been explained with increased glycosylation of erythrocyte membrane proteins [17]. Increased lipid peroxide production and membrane protein oxidation in diabet causes hemolysis of RBC resulting from hyperglycemia. Lipid peroxidation of RBC membranes increases membrane rigidity, cellular deformability, and reduce erythrocyte survival and lipid fluidity. It has been noted that the anemia in diabetes can be associated glomerular filtration rate, urinary albumin excretion rate, and glycated Hb (HbA1c) levels [6,21]. The other cause of anemia in diabetes has been suggested reduced erythropoietin production in kidneys. Although MCV, MCH and MCHC showed slightly fluctuation and these changes were no important in all groups. Thus the changes in MCV, MCH and MCHC can be considered as related to RBC, Hb and Htc levels in our study.

In the study Hb and Htc levels were found to be higher in DQ group compared with D group. RBC and Htc levels tended to increase in DQ group. The changes above can be attributed to beneficial effects of quercetin. It has been reported that quercetin have many biological properties including antioxidant, antiinflammatory activities[1]. Kim et al.[10] observed a reduction in serum glucose levels and glycated hemoglobin in diabetic mice received quercetin. It has been reported that quercetin has positive effect against STZ induced damage in  $\beta$  cells [1,4] . At the same time Ohlsson and Aher[15] stated that flavonoids can stimulate secretion of erythropoietin and stimulate stem cells to produce red blood cells. Also Riviera et al. [19] observed that quercetin improved insulin resistance in genetically obese Zucker rats. In our study the obtained increases in Hb, RBC, Htc in DQ group could be based to the results stated above.

In the study platelet count significantly decreased in diabetic rats compared with C and Q groups. This reduction in diabetic rats indicates suppression of haemopoiesis as a result of STZ application and hyperglycemia. On the other hand there was no significant change in platelet counts of DQ group with quercetin treatment although platelet counts slightly increased.

In our study WBC count and neutrophil percentage significantly increased with diabetes. The same parameters in DQ group tended to increase insignificantly compared to D group. The mechanism of leukocytosis in diabetes is exactly unknown. However leukocytosis in diabetes may be activated through the release of cytokines such as TnF $\alpha$ , transforming growth factor 1, nuclear factor kappa B (NF-kB) [14,7,8,20]. Also Pertynska- Marczevska et al. [18] reported that leucocytes can be activated by advanced glycation end products and oxidative stress in diabetes. Kozlov et al.[12] reported moderate neutrophilic leukocytosis and prolonged circulation times of neutrophils and monocytes in diabetic mice and suggested that count may also show low-grade inflammation. The above studies have supported the increase in diabetic rats in our study. Although some studies[1,13] reported that high level quercetin treatment decreased leucocyte count. In our study quercetin, at least this amount, did not significantly affect the leucocyte count in DQ group compared with D group.

In conclusion our results showed that further studies are needed about quercetin and its effects on diabetes with amount and duration.

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