Effect of alcoholic bilberry (Vaccinium arctostaphylos) extracts adhered to ZnO nanoparticles on oxidative stress in Wistar diabetic Male rat**Abstract:**

Background: Oxidative stress, caused by an imbalance between the content of antioxidants and free radicals in the body, is one of the causes of other diseases, including diabetes. The paraoxonase 1 and superoxide dismutase enzymes, malondialdehyde, as well as total antioxidant capacity, are part of the antioxidant defense of the body. Zinc oxide, which is a mineral compound, is a nanoparticle that has a better entry into the body. The vaccinium arctostaphylus plant also contains various organic antioxidants.

Aim:The aim of this study was to investigate the effect of ethanol extract of ZnO nanoparticles on oxidative stress in diabetic male rats.

Materials and Methods: In this experimental study, 30 male Wistar rats were utilized randomly to form six groups. In nondiabetic group C (control group), each rat received intraperitoneal injection of 1 mL of 0.9 %NaCl saline solution. In diabetic group E (Extract), a single dose of 150 mg/kg of vaccinium arctostaphylos extract was given. In diabetic group Ins (Insulin), a single dose of 10 U/kg was given. In diabetic group N (None), each rat received intraperitoneal injection of 1 mL of 0.9 %NaCl saline solution. In diabetic group NE (Nanoparticle-Extract), a single dose of 8 mg/kg was given. In diabetic group NP (Nanoparticle), a single dose of 8 mg/kg was given. Diabetes induction was performed with an intraperitoneal injection of alloxan monohydrate. After confirmation of diabetes induction, treatment period was performed for 16 days. Blood samples were taken before and after treatment for biochemical studies and liver tissue was used to evaluate the expression of paraoxonase 1 gene by PCR-Real Time. T-test and Kruskal wallis were used for analysis.

Results: The results showed that PON1 gene expression in NE group compared to E, Ins and C group was significantly increased ($p < 0.05$). Injection of zinc oxide nanoparticles synthesized by vaccinium arctostaphylos extract, zinc oxide nanoparticles, insulin and vaccinium arctostaphylos extract in male Wistar rats caused a significant increase in total antioxidant capacity, malondialdehyde and paraoxonase1 and serum supraoxydistidase enzymes in comparison to diabetic control group ($05.0 > p$). Total antioxidant capacity, malondialdehyde, paraoxonase and superoxide dismutase enzymes in serum after injection of zinc oxide nanoparticle synthesized by vaccinium arctostaphylos extract, zinc oxide nanoparticles, insulin, and vaccinium arctostaphylos extract in diabetic male rats decreased significantly compared to pre-injection, mostly in None group compared to others. ($p < 0.05$).

Conclusion: Injection of zinc oxide nanoparticle synthesized by vaccinium arctostaphylos extract can significantly increase the PON1 gene expression in diabetic male wistar rats compared to other treatments examined. Zinc oxide nanoparticles synthesized by vaccinium arctostaphylos extract, zinc oxide nanoparticles, insulin and vaccinium arctostaphylos extract in diabetic male Wistar rats can cause a significant increase in serum total antioxidant capacity and serum paraoxonase 1 and superoxide dismutase enzymes which can be a pathway protecting against oxidative stress in diabetic male wistar rats.

Keywords: Diabetes, Antioxidant defense, Oxidative stress, Paraoxonase 1, Rat