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Vaccinium Myrtillus (Blueberry) Ekstraktı Verilen Ratlarda Bazı Hematolojik ve Biyokimyasal Parametrelerin Araştırılması

Investigation of Some Hematological and Biochemical Parameters of Rats Were Given *Vaccinium Myrtillus* (Blueberry) Extract

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ÖZ

Amaç: Bu çalışmada, *Vaccinium myritillus* (yaban mersini) ekstraktı ile beslenen ratların hematolojik ve biyokimyasal parametrelerinde meydana gelen değişiklikler araştırıldı.
Yöntem: Araştırmada hayvan materyali olarak rat kullanıldı. Ratlar, her grupta 10 adet olacak şekilde 2 ayrı gruba ayrıldı. Kontrol grubundaki ratlar ad libitum beslenmeye tabi tutuldu. Deneme gurubuna ise 8 hafta süreyle yaban mersini ekstraktı 20 mg/kg oranında içme sularına karıştırılarak verildi. Biyokimyasal parametrelerden albumin (Alb), alkalen fosfataz (ALP), alanin aminotransferaz (ALT), amilaz (AMY), kan üre nitrojen (BUN), kalsiyum (Ca^{++}), kreatinin (CRE), potasyum (K^{+}), sodyum (Na^{+}), fosfor (Phos), total bilurubin (TBIL), total protein (TP), açlık kan şekeri (FG), total kolesterol (TK); hematolojik parametreler olan WBC, LYM, MON, NEU, LY, MO, NE, RBC, HGB, HCT, MCV, MCH, MCHC, RDW PLT, PCT, MPV, PDW değerlerine bakıldı.
Bulgular: Deney süreci tamamlanıp, kan örnekleri alındıktan sonra yukarıdaki parametreler arasından; Kreatinin: 0.48'den 0.41'e düştü. MPV: 6.48'den 6.30'a, PDWc: 33.40' dan 32.48 düzeyine düştü. Bu parametrelerin dışında kalan parametrelerde anlamlı bir değişiklik gözlenmedi.
Sonuç: Yaban mersininin kan parametreleri üzerinde olumsuz bir etkisinin olmadığı, aksine MPV ve PDW değerlerindeki anlamlı düşüş nedeniyle damar sertliği için bir risk faktörü olan oksidatif zarar sonucu parçalanmış trombositlerin atardamar çeperlerine yapışmasını ve arteroskloroz riskini de azaltabileceği düşünülebilir.

Anahtar Kelimeler: Biyokimyasal belirteçler, kan testleri, rat, *Vaccinium myrtillus.*

ABSTRACT

Objective: In this study, the differences in hematological and biochemical parameters were investigated in rats given *Vaccinium myrtillus* (blueberry) extract.
Methods: Biochemical parameters albumin (Alb), alkaline phosphatase (ALP), alanine aminotransferase (ALT), amylase (AMY), blood urea nitrogen (BUN), calcium (Ca), creatinine (CRE), potassium (K), sodium (Na), phosphorus (Phos), total bilirubin (TBIL), total protein (TP), fasting glucose (FG), total cholesterol (TC), and hematologic parameters such as WBC, LYM, MON, NEU, LY, MO, NE, RBC, HGB, HCT MCV, MCH, MCHC, RDW, PLT, PCT, MPV, PDW levels were measured. In the study, rats were used as animal material. The rats were separated into two groups, each of which included 10 rats. Ad libitum fed rats were subjected to the control group. In the group of blueberry extract for a period of 8 weeks of the experiment the rate of 20 mg/kg were mixed with drinking water.
Results: Completion of the process of the experiment, after obtaining blood samples from the above parameters, creatinine: 0.48 from 0:41 to fell in value. MPV: 6.48 from 6.30 a, PDW: 33.40 from the 32.48 level have fallen. But no significant changes were observed outside of these parameters.
Conclusion: As a result, there is a negative impact on blood parameters of blueberry on the contrary due to the significant decrease in the values of MPV and PDW, which is a risk factor for hardening of the arteries as a result of oxidative damage fragmented platelets sticking to the walls of arteries and reduce the risk of atherosclerosis be considered.

Key Words: **:** Biochemical markers, hematological tests, *rat, Vaccinium myrtillus.*

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1. INTRADUCTION

The relationship between healthy foods and healthy life is getting more significant every day. Consequently, for a healthy nutrition and diet, consumers are becoming more interested in healthy, natural and delicious products that are grown in natural environments and not contaminated with drugs and chemicals (1).

Phytochemicals are becoming more significant because free oxygen radicals play a key role in the development of chronic diseases. Fresh vegetables, fruits and grains have more than 9,000 antioxidant phytochemicals (2). Greater oxidative stress harms large biomolecules. The risk for coronary artery, metabolic syndrome and cancer diseases increases as basic cellular components such as proteins, DNA, lipids and lipoproteins are damaged. Consuming vegetables and fruits containing plenty of phenol and carotenoid protects against oxidative stress and reduces the risk for chronic diseases (3, 4).

Blueberries are protective against certain chronic diseases such as cancer, cardiovascular and cerebrovascular diseases, atherosclerosis and diabetes, and beneficial for health, which can be explained by anthocyanidin's high antioxidant capacity (5, 6).
The color of blueberries, which is dark blue or purple, is generated by anthocyanidin pigments. Many of its biological characteristics are related not only to the anthocyanidin pigments, but also to antioxidant activities (7, 8). These antioxidants can be used to neutralize degenerative diseases, the conditions of which depend on specific developments, and free radicals that are unstable molecules (9).

Laboratory studies have indicated that the polyphenols in blueberries boost the resistance of red blood cells to oxidative stress (10). In addition, blueberries contain ellagic acid and resveratrol, which are significant anticarcinogenic substances (11)
Recently, research on blueberries has focused on potential value in the treatment or prevention of conditions associated with inflammation, antimicrobial activity dyslipidemia, hyperglycemia or increased oxidative stress, cardiovascular disease (CVD), cancer, diabetes, and dementia and other age-related diseases. Studies on blueberries were carried out until daylight, but just a few studies were found to investigate the interaction of blueberries with hematological and biochemical parameters in the literature reviews. For this reason, this study was planned to investigate the effect of blueberries on blood parameters.

2. MATERIALS AND METHODS

The study material consisted of 20 Wistar albino rats, the live weights of which ranged between 200 and 250 grams. The rats were provided by the Experimental Animals Unit at Yüzüncü Yıl University. Prior to the experiments, the rats were fed ad libitum and had access to drinking water during the adaptation process. The rats were fed using special rat feed. The study was conducted after the permission of local ethics committee was obtained. The rats' adaptation was ensured in seven days in an environment which was illuminated for 12 hours and dark for the rest of the day. The temperature of the environment was 22±1°C, and the humidity rate was 60%. The rats were separated into two groups, each of which included 10 rats.

1. Control group: The rats in this group were fed ad libitum for eight weeks. No further action was performed.
2. Experimental group: The rats in this group were administered *Vaccinium myrtillus* extract (20 mg/kg) once a day (added to their drinking water). This routine continued for eight weeks and the feeding of rats would be adlibitum.

Blueberry Extract taken from https://www.alibaba.com › Health & Medical › powder. GMP Certified Manufacturer Supply Blueberry Extract powder 25% Anthocyanin Uv-vis (ep/cn standard), prepared by Solvent Extraction method, Hangzhou Greensky Biological Tech Co., Ltd, China.

Blood samples were taken from the animals under anesthesia. Hematological parameters were examined using Abacus Junior Vet 5(Diatron) at the Physiology Department of the Faculty of Veterinary Medicine. Biochemical parameters were examined using VetScan2 Autoanalyzer (Modüler pp, Roche) at the laboratory of the Biochemistry Department of the Faculty of Veterinary Medicine.

Statistical analysis

Descriptive statistics—means, standard deviations, minimum and maximum values—were used for data by the study. In addition, Student's *t* test was used to compare the groups' mean values. To determine the relationship between these values, Pearson's correlation coefficient was calculated. The threshold for statistical significance level was considered to be 5% in the calculations, and SPSS statistical package program was used for this purpose (12).

3. RESULTS

Biochemical parameters are presented in Table 1, hematological parameters are presented in Table 2. Regarding the serum MPV and PDW values, a statistically significant difference was found between the control group and other groups to which the extract was administered ($p < 0.05$).

Table 1. Descriptive Statistics and Comparison Results for Groups by Biochemical Parameters

Parameters*	Experimental group S±SD	Control group S±SD
Alb(g/dl)	4.23±0.64	4.32±0.51
ALP (U/l)	135.37±29.77	110.42±38.02
ALT (U/l)	53.90±8.33	53.43±7.31
AMY (U/l)	1983.60±192.34	1872.46±212.19
TBIL(mg/dl)	0.09±0.03	0.09±0.04
BUN (mg/dl)	14.79±0.85	15.19±1.25
Phos (mg/dl)	6.66±0.73	6.47±1.17
FG (mg/dl)	133.40±17.19	133.30±17.11
Ca^{++} (mg/dl)	10.18±0.31	10.21±0.28
Cholesterol	53.11±5.25	56.43±6.34
CRE (mg/dl)	0.41±0.04	0.48±0.07
K^{+}(mEq/l)	4.41±0.32	4.31±0.35
TP (g/dl)	7.43±0.47	7.60±0.42
Na^{+}(mEq/l)	142.64±1.11	143.09±1.67

All parameters represented as means±standard deviation. *Means in the same line with different superscript letters are significantly different at $p<0.05$.

Table 2. Descriptive Statistics and Comparison Results for Groups by Biochemical Parameters

Parameters*	Experimental group S±SD	Control group S±SD
WBC(x1000)	8.03±3.37	8.08±3.89
LYM(%)	6.64±2.97	6.31±2.91
MON(%)	0.19±0.18	0.28±0.50
NEU (%)	1.21±0.55	1.49±0.80
LY (%)	82.14±5.35	78.26±6.03
MO (%)	2.96±3.16	3.54±4.74
NE (%)	18.19±2.80	18.22±2.83
RBC(10^6)	8.55±0.69	8.21±0.90
HGB (g/dl)	14.18±0.76	13.59±0.92
HCT (%)	44.87±2.81	42.39±4.20
MCV(μm^3)	52.50±1.78	51.80±2.30
MCH(pg)	16.63±0.84	16.67±1.59
MCHC(g/dl)	31.64±1.41	32.24±2.97
RDW (%)	15.62±0.71	15.99±0.44
PLT(x1000)	652.20±47.33	694.20±124.18
PCT (%)	0.42±0.04	0.44±0.08
MPV (fL)	**6.30**±0.13*	**6.48**±0.16
PDW (fL)	**32.48**±0.86*	**33.40**±0.63

All parameters represented as means±standard deviation. *Means in the same line with different superscript letters are significantly different at $p<0.05$.

MPV values in the rats to which *Vaccinium myrtillus* was administered were found to decrease in the control and experimental groups, and a statistically significant difference was found ($p<0.05$).

Regarding the mean platelet distribution width (PDW) value in the rats to which *Vaccinium myrtillus* was administered, a statistically significant difference was found between the experimental and control groups ($p<0.05$). Moreover, *Vaccinium myrtillus* was effective on blood PDW value. A positive correlation was present between PDW and MPV values ($p<0.05$). Thus, the decrease in MPV value explains the decrease in PDW value.

4. DISCUSSION

Hypertension, supported by the vessels and kidneys, is a high-risk factor for cardiovascular diseases. Oxidative stress indicators such as proteinuria and renal nitrites diminished in the rats fed with cranberry, indicating that cranberry protects against renal diseases (13, 14). Blueberry contains plenty of antioxidants, which supports the hypothesis that a diet enriched with blueberries may slow down the development of hypertension in rats that are prone to suffer from hypertensive paralysis (15).

Morazzoni et al. (1991) observed that antocyanosite component in V. myrtillus rapidly spread after it was administered to male rats, and it was dissolved after it mixed with blood using the three-compartment pharmacokinetic model. Elimination was ensured through urine or gall with 5% absorption. Antocyanosite plasma concentration reached the maximum level fifteen minutes after the oral dose and started to decrease two hours later.

Creatinine value was found to fall from 0.48 to 0.41 in this study. A fall of this value does not have clinical significance. However, Vaccinium myrtillus may reduce this value in diseases such as renal failure, which has high creatinine levels. In addition, no statistically significant difference regarding the biochemical parameters such as albumin serum, ALP, ALT, amylase, bilurubin, BUN, phosphorus , fasting glucose, Ca serum, fasting cholesterol, K serum, total protein serum and Na serum was found between the control and experimental groups, and these values resemble those in the literature (17).

Funke and Melzig (2005) evaluated the use of plant-based alpha-amylase inhibitors in antidiabetic treatment. They reported that plant-based alpha-amylase inhibitors are capable of reducing the postprandial blood sugar and can be used in diabetes treatment. The actual components that inhibit alpha-amylase activity are polyphenolic components.

Another study suggested that *Vaccinium myrtillus* was effective in reducing the blood cholesterol level, and the antioxidant effects were effective in ensuring that malign cholesterol and cardiovascular diseases do not cause paralysis (19).

A study examining the effect of flavonoid intake by Korean women who were over 30 on reducing the T2DM and KVH risks (20) suggested that flavonoid intake over 25% was negatively related to systolic blood pressure, triglyceride, TG/HDL-cholesterol and insulin resistance.

Bao et al. (2008) administered *Vaccinium myrtillus* and vitamin C orally to rats for five days before they were kept hungry for 18 hours, and they took tissue and blood samples following the hunger stress. Plasma ALT and MDA values were at the lowest, and liver GSH and vitamin C amount were at the highest amount. The MDA level was in the lowest group in the rats being fed with cranberry at 200 mg/kg/day.

In a study that examined the effect of flavonoid intake on the endothelium functions of males, cranberry consumption improved acute vascular functions, depending upon the time and intake rate of the males. This explains the mechanism of dependence on the actions of phenolic metabolites in the circulation on neutrophile NADPH oxidase activity (22).

Riso et al. (2013) reported in their studies, which examined the effect of regular WB or placebo (PL) drink consumption on the oxidative stress, inflammation and endothelial functions with cardiovascular disease risk, that consuming WB drink for six weeks boosted resistance to oxidatively-induced DNA damage and significantly reduced levels of oxidized DNA bases.

Moreover, an inverse relationship was also found between the increase in flavonoid intake and coronary cardiac diseases. The reason for this relationship is that flavonoids are antioxidant, antithrombotic, anti-inflammatory and antiproliferative (24, 25, 26).

Physiological parameters such as WBC, LYM, MON, NEU, NE%, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT and PCT did not change, and these values were normal (17, 27). A study indicates that *Vaccinium myrtillus* extract affects the aorta tissue and cellular signal transmission in rats, may improve advanced cardiac and arterial health and caused cellular changes (28).

Anthocyanins and proanthocyanins may be effective in maintaining the integrity in the capillary vessel of rats that are exposed to oxygen toxicity (29). Anthocyanins reduce the risk for coronary cardiac diseases, inhibit platelet aggregation and protect artery cells (16, 25). Flavonoid intake was found to be inversely correlated with CV risk, non-fatal CV events and mortality based on all reasons in a cohort with low consumption rates of soy, tea and cacao, which are considered foods that have flavonoid-related benefits (30).

In a study performed with seriously overweight healthy males, consumption of acai berry was related to progress in vascular function. It may reduce the risk for cardiovascular diseases. In addition, the total amount of peroxide, which is an indicator of oxidative stress after acai consumption, increased at a significantly lower rate (31).

MPV values indicate the dimensions of platelets. An increase in MPV values indicates an increase in the diameters of platelets. High amounts of MPV increase the risk of coronary cardiac diseases and paralysis. Since young platelets are large and have greater aggregation (combination) strength, the vessels can be blocked more easily. Studies conducted in recent years have indicated that mean platelet volume increased in acute myocardial infarct, unstable angina pectoris, ischemic cardiac diseases and congestive cardiac failure (32).

MPV values in the rats to which *Vaccinium myrtillus* was administered were found to decrease in the control and experimental groups, and a statistically significant difference was found ($p<0.05$). Prevention of coronary diseases is quite important because this decrease in MPV value does not cause thrombocytopenia (platelet deficiency). Prevention of platelet aggregation complies with the literature since it protects blood vessels, particularly the arteries (4, 25).

5. CONCLUSIONS

It is fair to say that *Vaccinium myrtillus* does not have any negative effects on blood parameters, and it can diminish the risk for platelets, which are divided due to oxidative damage, a risk factor for arteriosclerosis, to get stuck on arterial walls because of the significant decrease in MPV and PDW values and the consequent antithrombotic effect. An inverse relationship was found between increased flavonoid intake and coronary cardiac disease. In addition, this study suggests that phenolic substances in *Vaccinium myrtillus* can be used to protect blood vessels, and this study will be useful for future studies.

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