Table 4
Compatibility of actual and expected results of 146S particle concentration determination by spectrometric method with rtRT-PCR and CFT ($n_{tests} = 3$)

Таблица 4
Степень совпадения фактических и ожидаемых результатов спектрометрического способа определения концентрации 146S частиц с ОТ-ПЦР-РВ и РСК ($n_{иссл.} = 3$)

Sample status	FMDV strain	Number of samples	Compatibility of spectrometric method results with other methods, %	
			rtRT-PCR [7]	CFT
test samples	A/Turkey/2006	40	97.0–99.4	96.2–97.1
	A/ARRIAH/2015	40	96.8–99.3	94.9–97.0
	O/Primorsky/2012	40	98.3–99.2	97.2–98.5
	O/Primorsky/2014	40	98.0–99.3	97.0–98.1
	Asia-1/Tajikistan/2011	40	98.4–99.5	97.6–98.5
	C_1/Zakarpatsky/1972	40	97.0–97.7	95.2–97.1
	SAT-1/Akhalkalaksky/62	40	96.1–97.3	94.8–96.0
	SAT-2/Saudi Arabia 7/2000	40	98.0–99.1	96.5–98.2
	SAT-3/Bechuanaland 1/65	40	97.9–98.5	94.5–97.9
positive control	Asia-1/Tajikistan/2011	40	99.2–99.6	99.0–99.3
negative control	–	40	100	100

demonstrated 99.0–99.6% compatibility of actual and expected results. FMDV genome and 146S particles were not detected in the negative control, and that was in line with expectations.

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Investigation of healing effects of Afyonkarahisar Region thermal spring water on experimentally-induced nephritis in mice

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SUMMARY

The aim of this study was to determine the efficacy of Afyokarahisar termomineral water in the treatment of nephritis. For this purpose, 40 Albino mouse at the same daily age were used. Nephritis was induced by adding adenine to their feed at a rate of 0.2% for 6 weeks. After nephritis was induced, a 21-day treatment period was started, and the mice were equally divided into two groups as control and study. While control group mice were received tap water daily and bathing in tap water, study group animals were given fresh Süreyya I hot spring water daily and bathing in this water. Clinical, hematological, blood biochemical and histopathological examinations were performed before the study, after nephritis formation, and on days of 1st, 7th, 14th and 21st of treatment period. Results of this study showed that WBC, NEUT and MCV levels increased significantly ($p < 0.05$) following nephritis formation, while RBC, HB, HCT, LYM, MCH and MCHC levels decreased significantly ($p < 0.05$). It was also determined that AST, GGT, GLU, BUN and IgG levels of blood biochemical parameters were significantly increased ($p < 0.05$) and TP, ALB levels decreased significantly ($p < 0.05$) after nephritis formation. At the end of the study, it was seen that all the measured parameters turned to the normal range in the study group animals, whereas problems still continuing with control group animals. Consequently, it was concluded that Süreyya I hot spring water was very successful in the treatment of nephritis and considered as an option in the treatment of nephritis.

Key words: Afyonkarahisar, balneotherapy, biochemistry, mouse, nephritis, treatment.

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Исследование лечебного действия термальной воды региона Афьонкарахисар на экспериментально индуцированный нефрит у мышей

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РЕЗЮМЕ

Целью настоящего исследования является определение эффективности применения термоминеральной воды региона Афьонкарахисар в лечении нефрита. Для этой цели использовали 40 мышей-альбиносов одного возраста. Нефрит воспроизвели путем добавления аденина в их корм из расчета 0,2% на протяжении 6 недель. Перед началом 21-дневного курса лечения минеральной водой индуцированного нефрита мышей разделили на две равные группы: контрольную и экспериментальную. Животных контрольной группы ежедневно выпаивали водопроводной водой и купали в ней, животным экспериментальной группы ежедневно давали свежую воду из горячего источника Süreyya I, а также устраивали ежедневные ванны с использованием этой воды. Клинические, гематологические, биохимические и гистопатологические исследования проводили до исследования, после развития нефрита, а также на 1, 7, 14 и 21-й день эксперимента. Полученные результаты показали, что после развития нефрита уровни лейкоцитов (WBC), нейтрофилов (NEUT) и среднего объема эритроцитов (MCV) в крови значительно увеличились ($p < 0,05$), в то время как уровни эритроцитов (RBC), гемоглобина (HB), гематокрита (HCT), лимфоцитов (LYM), среднее содержание гемоглобина в эритроците (MCH) и средняя концентрация гемоглобина в эритроците (MCHC) значительно снизились ($p < 0,05$). Также было установлено, что после развития нефрита уровни аспартатаминотрансферазы (AST), гамма-глутамилтрансферазы (GGT), глюкозы (GLU), содержание азота мочевины в крови (BUN) и уровень IgG значительно повысились ($p < 0,05$), а уровни общего белка (TP) и альбумина (ALB) значительно снизились ($p < 0,05$). В конце исследования у животных из экспериментальной группы все параметры крови нормализовались, тогда как у мышей контрольной группы такого эффекта не наблюдалось. Это позволило сделать вывод, что термальная вода из источника Süreyya I эффективна в лечении нефрита и может рассматриваться как один из вариантов терапии.

Ключевые слова: Афьонкарахисар, бальнеотерапия, биохимия, мышь, нефрит, лечение.

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INTRODUCTION

Kidneys are the organs that play an important role in metabolic activities such as absorption of minerals and water, the acid-base balance and the functionality of the buffer systems [1]. Nephritis is a condition in which nephrons, which are functional units of the kidneys, become inflamed which can adversely affect the kidney function [2].

It has been shown that people who use hot springs as balneotherapy have important benefits in endemic nephropathic cases [3]. So, P. B. Nocco reported that balneotherapeutic cures, including inpatient and bath therapies, were very important for regaining health, especially in the treatment of chronic cases such as nephritis [4]. In addition, alkaline mineral waters were used for the purpose of detoxification [5, 6]. A. L. Rodgers claimed that the calcium oxalate stones formed in the kidneys over time had achieved very successful results from the treatment with waters containing calcium and magnesium, and these waters had have effects not only for therapeutic purposes but also for prophylactic purposes [7]. R. Siener et al. reported that consuming water containing magnesium and bicarbonate similarly regulates urinary pH, magnesium and citrate excretion, prevents calcium oxalate stone formation and prevents increased calcium excretion [8].

In this study, it is aimed to reveal the importance of treatment with Süreyya I hot spring water with rich content in the borders of Afyonkarahisar Province in the treatment of experimental nephritis.

MATERIALS AND METHODS

The experimental part of this study was carried out in Afyon Kocatepe University Experimental Animals Application and Research Center, in accordance with the Directive of Afyon Kocatepe University Experimental Animals Ethical Committee (AKUHADYEK) and was referred to with the report numbered 59-18 of the board and supported by Afyon Kocatepe University Scientific Research Projects Board (AKÜBAPK) as the Master's Thesis with Project number 18.SAĞ.BİL.12.

Animal Material. In this study, 40 Albino mice of the same age were used. Mice were kept in a stable environment under equal heat and humidity conditions, 12 hours day and 12 hours night, in Afyon Kocatepe University Experimental Animals Application and Research Center. Throughout the experiment, all the animals were fed *ad libitum* food.

Creating Experimental Nephritis. Four of the 40 mice were exempted to take blood samples before performing the nephritis procedure in all animals. Nephritis was created in remaining mice by adding 0.2% adenine to their food for 6 weeks [9]. After the nephritis was created, 4 out of 36 mice were ex for collecting blood and histopathological examinations, and the remaining 32 mice with nephritis were divided equally and randomly into 2 groups as below:

1. Control Group (CG). Tap water was added to the drinkers of 16 mice with nephritis, and they were provided with access to refreshed water and food *ad libitum* every day. All the mice in CG were bathed with tap water at (35 ± 2) °C for 15 minutes at the same time once a day up to end of this study, which was 21 days.

2. Study Group (SG). Fresh hot spring water was added to the drinkers of 16 mice with nephritis, and it was provided to reach the refreshed daily hot spring water and food *ad libitum*. All the mice in SG were bathed with fresh hot spring water at (35 ± 2) °C for 15 minutes at the same time once a day.

Süreyya I hot spring water, used for treatment in this study, has a total mineral content of 4046.8 mg/L, and it is in the thermomineral water group with sodium bicarbonate, carbon dioxide, magnesium, calcium, fluoride and silicon.

Clinical Examinations. Respiratory rates (R), body temperatures (T) and heart frequencies (P) were measured in all of the mice used in the study, and the results were recorded for statistical comparisons.

Collecting Blood and Tissue Samples. Blood and kidney tissue samples were exhausted under ketamine/xylazine (100/10 mg/kg) anesthesia [10] before the study, after nephritis formation (NF), and on 1st, 7th, 14th and 21st days following the treatment period.

Hematological Examinations. In blood samples; total leukocytes (WBC), lymphocytes (LYM), hemoglobin (HB), mean corpuscular volume (MCV), hematocrit (HCT), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), neutrophil (NEUT), eosinophil (EOS), erythrocytes (RBC), monocytes (MON) and basophils (BAS) were measured using Chemray Brand blood count commercial test kits (Rayto Life and Analytical Sciences Co., China).

Blood Biochemical Examinations. Blood urea nitrogen (BUN), serum aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), total protein (TP), glucose (GLU) were measured in Cobas Integra 400 Plus (Roche Brand (Roche Diagnostics GmbH, Germany) analyzer. Immunoglobulin G (IgG) levels were determined with ChemWell, Chromate 4300 Elisa Reader device (Awareness Technology, Inc., USA) using commerical Elisa kits (Sunred Biological Technology Co., Ltd, China).

Blood Gases Examinations. After taking blood samples to 500 IU liquid heparin plastic syringes for 1 ml of blood, which were prepared simultaneously with histopathological sampling, the tip of the sterile syringe was closed immediately, and measurements were made before < 3 hours. In blood samples partial carbon dioxide pressure (pCO_2), pH, total carbon dioxide concentration (TCO_2), bicarbonate (HCO_3^-), base deficit (BE), potassium (K^+), sodium (Na^+), chlorine (Cl^-), calcium (Ca^{2+}) values were made using a portable blood gas analyzer EDAN i15 Vet (EDAN Instruments, Inc., China) using commercial cartridges.

Histopathological Examinations. Obtained kidney samples by method mentioned above were sent to the Veterinary Control Central Research Institute, Pathology Laboratory to perform histopathological examinations in 10% formol, where 5 micron thick sections were taken, stained with hematoxylin-eosin and examined in a light microscope.

Statistical Analyses. Statistical calculations for CG and SG were made in accordance with the variance analysis (ANOVA) method. The Duncan's test was used to determine the significance of the difference in the groups. Statistical analyzes were provided through the Windows-compatible SPSS Statistics 18.1 (IBM, USA) package program. The data levels obtained are presented as mean ± standard error, and $p < 0.05$ is considered to be important.

Table 1
Statistical comparison of body temperature, pulse frequency and respiratory rate

Таблица 1
Статистическое сравнение температуры тела, частоты пульса и частоты дыхания

Time of indicator measurement by groups		Parameters (X ± SD)		
		T (°C)	P (frequence/min)	R (rate/min)
BS (n = 40)		37.10 ± 0.16^{b}	326.30 ± 44.22^{e}	117.04 ± 18.36^{f}
ANF (n = 36)		38.50 ± 0.14^{a}	327.31 ± 45.10^{e}	131.24 ± 25.43^{e}
AT 1st day	CG (n = 16)	38.50 ± 0.20^{a}	331.28 ± 33.40^{d}	132.54 ± 21.45^{e}
	SG (n = 16)	38.30 ± 0.18^{a}	363.14 ± 32.20^{b}	141.14 ± 22.25^{c}
AT 7th day	CG (n = 12)	38.30 ± 0.20^{a}	334.26 ± 27.20^{e}	135.30 ± 17.12^{d}
	SG (n = 12)	38.20 ± 0.10^{a}	378.23 ± 25.44^{a}	148.10 ± 15.23^{b}
AT 14th day	CG (n = 8)	38.20 ± 0.10^{a}	342.16 ± 22.23^{c}	137.10 ± 8.05^{d}
	SG (n = 8)	38.10 ± 0.12^{a}	374.25 ± 21.14^{a}	157.30 ± 7.20^{a}
AT 21st day	CG (n = 4)	38.10 ± 0.16^{a}	345.13 ± 9.21^{c}	142.18 ± 6.33^{c}
	SG (n = 4)	38.00 ± 0.10^{a}	376.44 ± 6.12^{a}	159.23 ± 4.22^{a}

$^{a–f}$ The values in the column are statistically significant ($p < 0,05$).

$^{a–f}$ Значения в столбце являются статистически значимыми ($p < 0,05$).

BS – before study (до исследования), ANF – after nephritis formation (после развития нефрита),
AT – after treatment (после лечения), CG – control group (контрольная группа), SG – study group (экспериментальная группа).

Table 2
Results of hematology blood tests

Таблица 2
Результаты гематологических исследований крови животных

Time of indicator measurement by groups		Parameters (X ± SD)											
		WBC (10^3/mm^3)	RBC (10^6/mm^3)	HB (g/dl)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)	LYM (%)	NEUT (%)	EOS (%)	MON (%)	BAS (%)
BS (n = 40)		8.38 ± 2.32^e	7.80 ± 2.32^b	13.53 ± 2.48^a	43.36 ± 5.32^a	55.04 ± 5.12^{bc}	17.19 ± 2.16^a	32.08 ± 2.43^a	60.50 ± 2.10^a	34.10 ± 4.14^f	2.30 ± 0.50	3.50 ± 0.40	NS
ANF (n = 36)		16.14 ± 4.10^a	5.34 ± 1.27^d	7.67 ± 3.34^e	31.37 ± 4.16^f	58.69 ± 5.24^a	14.38 ± 2.21^d	24.47 ± 3.06^d	47.84 ± 4.20^e	48.14 ± 5.28^a	2.56 ± 0.30	3.40 ± 1.50	NS
AT 1st day	CG (n = 16)	16.21 ± 4.20^a	5.31 ± 1.56^d	7.65 ± 3.16^e	31.43 ± 4.13^f	59.20 ± 5.32^a	14.43 ± 2.08^d	24.34 ± 3.32^d	47.34 ± 4.20^e	48.21 ± 4.16^a	2.68 ± 0.56	3.50 ± 0.40	NS
	SG (n = 16)	15.23 ± 3.04^{ab}	6.04 ± 1.47^{cd}	8.07 ± 3.14^{de}	32.78 ± 3.47^e	54.28 ± 5.16^c	13.35 ± 2.13^c	24.83 ± 3.02^d	47.30 ± 4.10^e	46.68 ± 4.25^b	2.34 ± 0.50	3.40 ± 0.30	NS
AT 7th day	CG (n = 12)	16.10 ± 2.42^a	5.48 ± 1.08^d	7.81 ± 2.06^e	32.14 ± 2.15^e	58.66 ± 3.27^a	14.28 ± 1.46^c	24.28 ± 2.36^d	47.32 ± 2.30^e	48.03 ± 2.38^a	2.54 ± 0.30	3.20 ± 0.30	NS
	SG (n = 12)	14.03 ± 2.05^b	6.78 ± 1.04^c	9.47 ± 2.03^c	38.22 ± 2.23^c	56.38 ± 3.41^b	13.94 ± 1.35^c	24.80 ± 2.48^d	53.38 ± 2.14^c	42.38 ± 2.43^c	2.10 ± 0.20	3.10 ± 0.30	NS
AT 14th day	CG (n = 8)	15.86 ± 1.23^{ab}	5.81 ± 0.68^c	8.02 ± 1.17^d	34.18 ± 1.54^e	58.82 ± 3.05^a	13.81 ± 0.43^c	23.44 ± 1.37^e	48.16 ± 1.30^e	47.30 ± 1.54^{ab}	2.42 ± 0.40	3.60 ± 0.30	NS
	SG (n = 8)	12.13 ± 1.17^c	7.74 ± 0.51^b	11.34 ± 1.09^b	41.45 ± 1.56^b	53.54 ± 3.20^{cd}	14.65 ± 0.52^c	27.39 ± 1.27^c	56.24 ± 1.14^b	39.34 ± 1.20^d	2.05 ± 0.20	3.00 ± 0.20	NS
AT 21st day	CG (n = 4)	14.86 ± 0.67^b	5.97 ± 0.44^b	8.57 ± 0.68^d	35.13 ± 0.67^d	58.83 ± 2.12^a	14.36 ± 0.34^c	24.40 ± 0.44^d	50.36 ± 0.68^d	45.23 ± 0.46^b	2.32 ± 0.10	3.80 ± 0.20	NS
	SG (n = 4)	9.23 ± 0.48^d	8.46 ± 0.37^a	13.01 ± 0.53^a	44.02 ± 0.54^a	52.03 ± 2.09^d	15.37 ± 0.41^b	29.56 ± 0.39^b	60.10 ± 0.57^a	36.03 ± 0.57^e	2.00 ± 0.10	2.60 ± 0.10	NS

[a–f] The values in the column are statistically significant ($p < 0{,}05$).

[a–f] Значения в столбце являются статистически значимыми ($p < 0{,}05$).

BS – before study (до исследования), ANF – after nephritis formation (после развития нефрита), AT – after treatment (после лечения),
CG – control group (контрольная группа), SG – study group (экспериментальная группа), NS – non-significant (не значимо).
WBC – white blood cells (лейкоциты), RBC – red blood cells (эритроциты), HB – hemoglobin (гемоглобин), HCT – hematocrit (гематокрит),
MCV – mean corpusculare volume (средний объем эритроцитов), MCH – mean corpuscular hemoglobin (среднее содержание гемоглобина в эритроците),
MCHC – mean corpuscular hemoglobin concentration (средняя концентрация гемоглобина в эритроците), LYM – lymphocyte (лимфоциты),
NEUT –neutrophils (нейтрофилы), EOS – eosinophils (эозинофилы), MON – monocyte (моноциты), BAS – basophils (базофилы).

TEST RESULTS

Since the mice had the same date of birth, there was no age difference in the mice ($p > 0.05$). The mean body weight (bw) before the study was calculated as 29.7 g, whereas it was calculated as 28.7 g after the NF, and a significant ($p < 0.05$) reduction was observed in terms of bw averages. On the 21st day of treatment, it was observed that mean bw of CG mice was 28.1 g, while that of SG mice was 29.1 g, and there was a statistically significant differences ($p < 0.05$) between CG and SG animals.

Clinical Findings

The clinical findings obtained during the study are shown in Table 1.

When Table 1 was examined, by nephritis formation, significant ($p < 0.05$) changes were seen in terms of body temperature, respiration and heart frequencies. So, mean R rates and P frequencies increased with the start of the treatment period, but this increase was more significant ($p < 0.05$) in the study group mice.

Hematological Findings

Hematological examination findings are shown in Table 2.

According to this table; NEUT, MCV, WBC levels were increased statistically significantly ($p < 0.05$) following NF, whereas HCT, HB, RBC, LYM, MCHC and MCH levels significantly decreased ($p < 0.05$). On the 21st day of the study, it was found that LYM, HCT, RBC, HB, MCH and MCHC levels increased in both groups, but NEUT, MCV, WBC levels decreased. These changes were statistically more significant ($p < 0.05$) in SG animals.

Blood Biochemical Findings

The blood biochemical analysis were shown in Table 3.

According to this Table; it was observed that GGT, AST, BUN, GLU and IgG levels increased significantly ($p < 0.05$) after NF, while ALB, TP and levels decreased significantly ($p < 0.05$). On the contrary, in the following days, TP, ALB levels were increased in both groups, whereas GGT, AST, BUN, GLU and IgG levels were decreased ($p < 0.05$). It was observed that the most significant differences occurred in SG mice in the last week of the study, and this difference was statistically significant ($p < 0.05$).

Blood Gases Findings

Blood gases analyses results were shown in Table 4.

When this table is examined, it was observed that pCO_2, pH, HCO_3^-, BE, TCO_2, Ca^{2+} and K^+ levels decreased

Table 3
Blood biochemical findings of the animals

Таблица 3
Результаты биохимических исследований крови животных

Time of indicator measurement by groups		Parameters (X ± SD)						
		AST (IU/L)	GGT (IU/L)	TP (g/dl)	ALB (g/dl)	GLU (g/dl)	BUN (mmol/L)	IgG (mg/ml)
BS (n = 40)		96.72 ± 12.38^h	3.63 ± 0.56^e	53.96 ± 5.47^b	33.78 ± 2.34^a	172.15 ± 0.69^d	21.74 ± 3.25^f	3.17 ± 1.45^e
ANF (n = 36)		269.17 ± 32.45^a	8.96 ± 3.43^a	34.06 ± 6.45^f	21.08 ± 3.44^e	275.27 ± 0.56^a	36.48 ± 5.23^a	8.16 ± 3.57^a
AT 1st day	CG (n = 16)	272.13 ± 42.34^a	8.97 ± 3.71^a	34.04 ± 6.48^f	21.01 ± 3.66^e	208.13 ± 0.30^a	37.04 ± 6.18^a	8.45 ± 3.44^a
	SG (n = 16)	263.12 ± 38.32^{ab}	8.78 ± 3.58^a	34.69 ± 5.17^f	22.23 ± 3.32^d	203.21 ± 0.44^b	36.91 ± 6.53^a	7.79 ± 3.08^b
AT 7th day	CG (n = 12)	253.25 ± 23.21^b	8.61 ± 2.45^a	34.23 ± 4.31^f	22.16 ± 2.54^d	196.11 ± 0.48^b	36.76 ± 4.21^a	8.17 ± 2.14^a
	SG (n = 12)	231.32 ± 19.34^c	7.41 ± 2.32^b	42.14 ± 4.32^d	26.34 ± 2.56^c	178.14 ± 0.53^c	28.64 ± 4.06^d	6.10 ± 2.03
AT 14th day	CG (n = 8)	234.07 ± 14.54^c	8.57 ± 1.37^{ab}	36.12 ± 3.21^{ef}	23.02 ± 1.21^{cd}	187.35 ± 0.48^c	34.17 ± 2.34^b	7.78 ± 1.34^b
	SG (n = 8)	162.44 ± 15.16^f	5.73 ± 1.44^c	48.16 ± 3.09^c	30.94 ± 1.41^b	173.43 ± 0.53^d	24.13 ± 2.11^e	4.32 ± 1.27^d
AT 21st day	CG (n = 4)	213.47 ± 10.21^d	7.32 ± 0.65^b	38.03 ± 1.53^e	25.21 ± 0.58^c	183.22 ± 0.10^c	30.14 ± 1.08^c	6.48 ± 0.65^c
	SG (n = 4)	103.34 ± 8.11^g	3.98 ± 0.59^d	56.05 ± 1.48^a	33.35 ± 0.49^a	166.17 ± 0.10^e	20.83 ± 0.53^f	3.15 ± 0.51^e

[a–h] The values in the column are statistically significant ($p < 0{,}05$).

[a–h] Значения в столбце являются статистически значимыми ($p < 0{,}05$).

BS – before study (до исследования), ANF – after nephritis formation (после развития нефрита),
AT – after treatment (после лечения), CG – control group (контрольная группа), SG – study group (опытная группа).
AST – aspartate aminotransferase (аспартатаминотрансфераза),
GGT – gamma-glutamyl transferase (гамма-глутамилтрансфераза), TP – total protein (общий белок),
ALB – albumin (альбумин), GLU – glucose (глюкоза), BUN – blood urea nitrogen (содержание азота мочевины в крови),
IgG – immunoglobulin G (уровень иммуноглобулина G).

Table 4
Blood gases findings of the animals

Таблица 4
Результаты исследования газового состава крови

Time of indicator measurement by groups		Parameters (X ± SD)									
		pH	pCO_2 (mmHg)	HCO_3^- (mmol/L)	BE (mEq/L)	TCO_2 (mmol/L)	LACT (mmol/L)	K^+ (mmol/L)	Na^+ (mmol/L)	Cl^- (mmol/L)	Ca^{2+} (mmol/L)
BS ($n = 40$)		7.32 ± 0.03^{b}	44.03 ± 0.42^{a}	21.91 ± 0.57^{b}	-3.3 ± 0.28^{b}	15.41 ± 1.58^{a}	4.68 ± 1.47^{cd}	8.78 ± 2.36^{a}	163.28 ± 14.18^{f}	117.34 ± 12.43^{g}	10.68 ± 2.09^{a}
ANF ($n = 36$)		7.22 ± 0.02^{d}	32.78 ± 2.14^{e}	13.02 ± 1.63^{de}	-13.1 ± 0.45^{f}	11.14 ± 2.27^{d}	7.03 ± 2.05^{a}	5.69 ± 2.21^{d}	264.32 ± 17.23^{a}	196.48 ± 13.44^{a}	6.47 ± 2.12^{c}
AT 1st day	CG ($n = 16$)	7.22 ± 0.02^{d}	32.68 ± 2.32^{e}	12.91 ± 1.43^{e}	-13.2 ± 0.44^{f}	12.05 ± 2.29^{c}	7.15 ± 2.28^{a}	5.58 ± 2.43^{d}	267.31 ± 13.21^{a}	193.57 ± 14.44^{a}	6.51 ± 2.23^{c}
	SG ($n = 16$)	7.23 ± 0.03^{d}	33.07 ± 2.48^{d}	13.64 ± 1.44^{e}	-12.4 ± 0.35^{e}	11.07 ± 2.33^{d}	6.87 ± 2.13^{ab}	5.31 ± 1.47^{d}	253.36 ± 18.25^{ab}	182.37 ± 12.24^{b}	6.89 ± 2.38^{c}
AT 7th day	CG ($n = 12$)	7.24 ± 0.02^{d}	33.78 ± 2.23^{d}	14.02 ± 0.68^{de}	-11.9 ± 0.34^{de}	11.70 ± 1.35^{a}	6.49 ± 1.68^{b}	5.37 ± 1.13^{d}	248.22 ± 15.12^{b}	181.38 ± 11.47^{b}	6.96 ± 1.43^{c}
	SG ($n = 12$)	7.30 ± 0.02^{bc}	37.48 ± 2.15^{bc}	17.82 ± 0.49^{c}	-7.5 ± 0.21^{c}	11.56 ± 1.47^{cd}	4.78 ± 1.37^{c}	6.22 ± 1.37^{c}	214.25 ± 13.27^{d}	158.34 ± 9.33^{d}	8.02 ± 1.35^{b}
AT 14th day	CG ($n = 8$)	7.27 ± 0.02^{c}	35.12 ± 1.54^{c}	15.61 ± 0.43^{d}	-10.1 ± 0.17^{d}	12.11 ± 0.66^{c}	6.54 ± 0.67^{b}	5.91 ± 0.68^{cd}	225.34 ± 11.11^{c}	164.33 ± 8.13^{c}	7.17 ± 0.76^{bc}
	SG ($n = 8$)	7.34 ± 0.03^{b}	42.02 ± 1.13^{b}	21.89 ± 0.31^{b}	-3.2 ± 0.14^{b}	14.80 ± 0.47^{cd}	4.22 ± 0.53^{c}	7.53 ± 0.67^{b}	178.35 ± 10.28^{d}	121.31 ± 7.35^{f}	9.49 ± 0.77^{ab}
AT 21st day	CG ($n = 4$)	7.30 ± 0.02^{bc}	36.87 ± 0.56^{bc}	17.52 ± 0.23^{d}	-7.7 ± 0.10^{c}	12.83 ± 0.39^{c}	6.04 ± 0.38^{b}	6.18 ± 0.43^{c}	203.44 ± 6.16^{e}	147.34 ± 5.14^{e}	8.06 ± 0.45^{b}
	SG ($n = 4$)	7.39 ± 0.02^{a}	44.13 ± 0.47^{a}	25.79 ± 0.19^{a}	-1.3 ± 0.10^{a}	15.82 ± 0.28^{a}	3.89 ± 0.39^{d}	8.99 ± 0.33^{a}	147.34 ± 5.22^{g}	103.42 ± 3.28^{h}	10.84 ± 0.38^{a}

[a–h] The values in the column are statistically significant ($p < 0,05$).
[a–h] Значения в столбце являются статистически значимыми ($p < 0,05$).
BS – before study (до исследования), ANF – after nephritis formation (после развития нефрита), AT – after treatment (после лечения),
CG – control group (контрольная группа), SG – study group (опытная группа).
pH – hydrogen ion concentration (концентрация ионов водорода), pCO_2 – CO_2 partial pressure (парциальное давление углекислого газа),
HCO_3^- – bicarbonate (бикарбонат), BE – base excess (сдвиг буферных оснований), TCO_2 – total CO_2 (общая концентрация углекислого газа),
LACT – lactate (лактат), K^+ – potassium (калий), Na^+ – sodium (натрий), Cl^- – chlorine (хлор), Ca^{2+} – calcium (кальций).

following NF, whereas LACT, Na^+ and Cl^- levels increased. However, with the onset of treatment period, a reverse course has taken shape in these parameters. On the other hand, it was observed that the most important changes in terms of these parameters occurred in SG animals in the last week of the study, and the difference was statistically significant ($p < 0.05$).

Histopathological Findings

In our current study, severe glomerulonephritis was detected in tissue sections taken from nephritic mice in which infiltration detected in the vascular lumen (Fig. 1).

It was found that there was almost a complete improvement in SG animals which treated with hot spring water at the end of the treatment period (Fig. 2), while CG animals which treated with tap water continued to show histopathological symptoms of nephritis in their kidney tissue sections (Fig. 3).

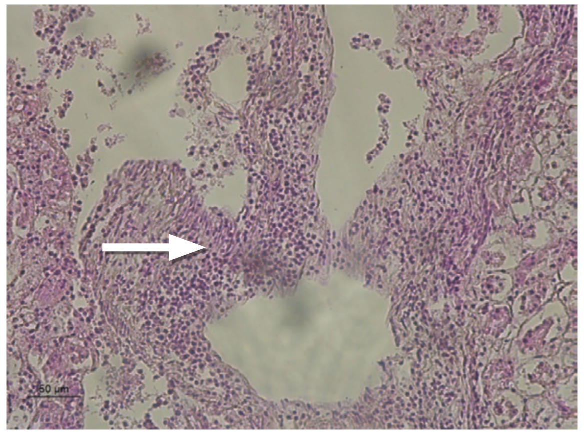

Fig. 1. Severe glomerulonephritis (white arrow), 10×–40×

Рис. 1. Выраженный гломерулонефрит (белая стрелка), увеличение 10×–40×

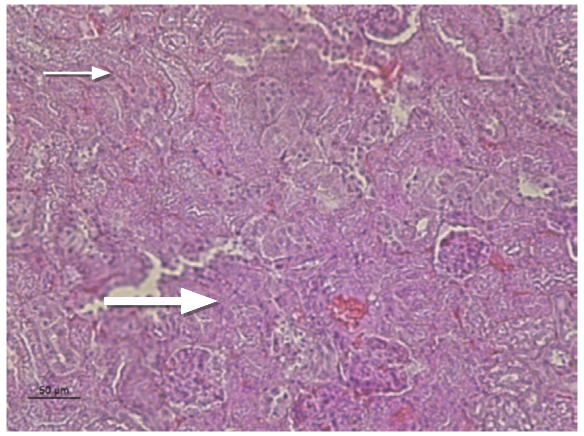

Fig. 2. Completely healed tubule and glomerul structure at the end of day 21 in study group animals (tubule – thin arrow, glomerul – thick arrow), 10×–20×

Рис. 2. Восстановление структуры канальцев и клубочков на 21-е сут у животных экспериментальной группы (канальцы – тонкая стрелка, клубочки – толстая стрелка), увеличение 10×–20×

DISCUSSION AND CONCLUSION

In this study, it was found that the mean of bw decreased with the NF, and this difference was found to be statistically significant ($p < 0.05$). On day 21st of the experiment the average bw of the CG mice was reported to be lower as compared to that of the SG mice ($p < 0,05$). These findings have been found to be compatible with study U. Lange et al., which reported that treatment with mineral waters supports fat breakdown and decreases the absorption of fat from the intestines, leading to a decrease in live weight [11].

It was found that the body temperatures increased in mice with nephritis, when compared to the pre-study, and this rising was statistically significant ($p < 0.05$). However, there was no significant ($p > 0.05$) changes in terms of R and P. With the initiation of treatment; it was observed that the levels for R and P increased in both groups, but the highest levels were shaped in SG animals. These findings support the findings of the researchers P. Greco-Otto et al., who reported that spa treatment increased heart rate, improvement in peripheral vessels, and an increase in heart and indirectly respiration rate [12]. Moreover, hot baths have been reported to stimulate the sympathetic nervous system, leading to an increase in blood pressure, heart and respiratory frequency [13].

It was observed that mean NEUT, WBC and MCV counts were continuing in high levels in CG animals, while SG mice which received Süreyya I hot spring water and bathed have a decreased. So, it has been reported that hyperthermal waters have an immunosuppressive effect and T-lymphocyte and EOS numbers decrease significantly in hyperthermal baths in both healthy individuals and those with chronic inflammatory disease [14].

It was found that mean RBC, HB, HCT, MCH and MCHC counts decreased statistically ($p < 0.05$) in the period following NF. It has been previously reported that these parameters decrease, the anemia table is shaped after nephritis, and this is due to a decrease in the production of erythropoietin produced in kidneys in rats with kidney damage caused by adenine [15]. The improvement in the red blood cell index after treatment in SG animals proves that Süreyya I hot spring water is extremely effective in terms of healing of kidney damage and anemic parameters. Furthermore, Süreyya I hot spring water is rich in Mg, and the inflammatory markers were low levels in SG animals by starting treatment period. As known, magnesium deficiency is one of the reasons specific clinical inflammatory syndrome, because its deficiency causes dyslipidemia, hypertension, insulin resistance, endothelial activation and prothrombic differences with the regulation of inflammation and oxidative stress markers [16].

In the current study, it was observed that GGT, AST, BUN and IgG levels increased significantly ($p < 0.05$) following NF, whereas ALB, TP and GLU levels decreased ($p < 0.05$). On the contrary, it was found that ALB, TP and GLU levels increased, whereas GGT, AST, BUN and IgG levels decreased by starting treatment period. On the other hand, the most important changes were seen in SG animals, and the difference was statistically significant ($p < 0.05$). Our these findings has been supported by the findings of researchers C. Pereira et al., who reported that UREA, ALT, AST, CREA levels decreased and TP and ALB levels increased as a result of consuming mineral

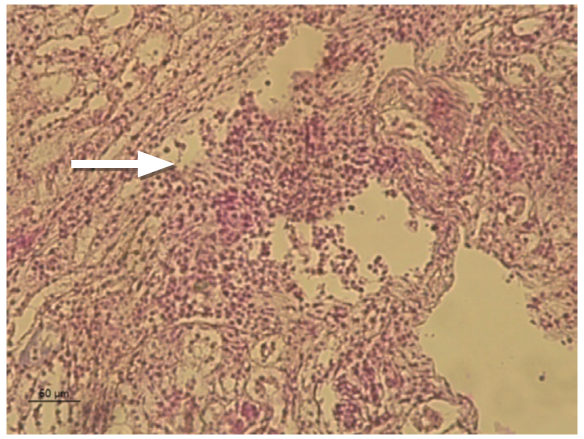

Fig. 3. Continuation of the glomerulonephritis structure at the end of day 21 in control group animals (white arrow), 10×–20×

Рис. 3. Гистопатологические признаки гломерулонефрита на 21-е сут в срезах почечной ткани животных контрольной группы (белая стрелка), увеличение 10×–20×

water in the experimental metabolic syndrome experimentally created by fructose [16]. Even though albumin levels decreased significantly following nephritis, it was thought to be related to liver damages, but it also indicated that there was no reabsorption from kidney tubules [17].

It has been explained that balneotherapy can be effectively applied to lower blood sugar levels. It has been reported that these beneficial effects of the balneotherapy might be related to its ability to control high blood sugar that causes glucose tolerance [18]. In the current study, GLU levels were high in nephritis-induced mice, but with the onset of treatment, the gradually decrease in GLU levels, the most important decreases were detected in SG mice, and these findings were consistent with these researchers reported above.

Unfortunately, we did not find a study measuring blood gases in the treatment of nephritis with hot spring waters in widely literature searches. In our study, it was observed that LACT, Cl^- and Na^+ levels increased significantly ($p < 0.05$) following NF, whereas Ca^{2+} and K^+ levels decreased. After the treatment was initiated, the opposite results were obtained, and it was determined that LACT, Cl^- and Na^+ levels decreased, while Ca^{2+} and K^+ levels increased. Compared with CG, these changes were seen to be faster and statistically more significant ($p < 0.05$) in SG animals. Hypercalcemic and hyperchloremic metabolic acidosis occurs after nephritis. Blood pH, HCO_3^- and pCO_2 levels decrease, Cl^-, Na^+ and LACT levels increase [19]. In addition to kidneys and lungs, mineral waters of suitable nature have been reported to provide acid-base balance in the liver and regulate the metabolism of LACT and some amino acids [20]. In the study, it was determined that the parameters mentioned in the 21st day of SG animals which treated with Süreyya I hot spring water, and reached physiological levels, and the metabolic acidosis case improved. So, L. Xu et al. previously reported that LACT levels significantly improved after 21 days of spa treatment in studies conducted in individuals living under bad conditions [19].

In our current study, severe glomerulonephritis was detected in the tissue sections of the kidneys of the mice with nephritis along with inflammatory infiltration in the vascular lumen (Fig. 1). Although a progressive improvement was observed in SG which treated with Süreyya I hot spring water at the end of this study (Fig. 2), it was observed that the nephritis picture continues in CG animals treated with tap water. These histopathological findings prove that the Süreyya I hot spring water provides significant improvements in the nephritis case histopathologically as well as clinical, hematological, blood biochemical and blood gasses findings.

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