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Results of the Study for the Antihypertensive Effect in the Panzeria Alaschanica Kupr Plant

Hu Bi Si Ha La Tu[1, 2], Khaliunaa Tumurbaatar[3], Chimedragchaa Chimedtseren[3], Tsogt Bukhbayar[2, 4], Tsend-Ayush Damba[2]

[1]Department of Internal Medicine, Medicine Hospital, Baotou, China; [2]Department of Mongolian Medicine, International School of Mongolian Traditional Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; [3]Research Center, Institute of Traditional Medicine and Technology, Ulaanbaatar, Mongolia; [4]Department of Internal Medicine, Affiliated Hospital of Inner Mongolia University For Nationalities, Inner Mongolia, China

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Corresponding Author
Hu Bi Si Ha La Tu, Department of Internal Medicine, Chinese Medicine Hospital, Baotou 014040, China.
Tel: +86-18686131926
E-mail: 13604777196@163.com

Objectives: To study the effect of the plant Panzeria alaschanica Kupr on lowering blood pressure. **Methods:** The experiment was performed using Sharon Leng Hong Ong (2009) using a male rat weighing 150 - 250 grams. On days 5, 8, 13, and 15 of the experiment, ECG, heart rate, and arterial pressure were measured in the rat's tail with a Neurobotic systole 1.2 instruments. At the end of the experiment, the content of renin, angiotensin II and aldosterone were determined by enzyme-linked immunosorbent assay. **Results:** According to the results of the study, the experimental group of plant Panzeria alaschanica Kupr ingested a dose of 160 mg/kg of renin 36.8 % compared with the control group that caused the pathological model, the amount of aldosterone in animals plant Panzeria alaschanica Kupr who ingested a dose of 32 mg/kg were 43.5 % of the ingested animals compared with the pathogenic group, the amount of angiotensin II in the plant Panzeria alaschanica Kupr was 64 mg/kg animals that ingested in, was reduced by a statistically significant difference ($p < 0.05$) of 34.3 % compared with the control group generated by the pathological model. **Conclusion:** Panzeria alaschanica Kupr has a 36.8 % reduced blood pressure by affecting the renin, angiotensin, and aldosterone systems.

Keywords: Traditional Chinese Medicine, Medicinal Plants, Arterial Blood Pressure, Dexamethasone, Captopril

Introduction

As of 2020, of the five leading causes of non-communicable disease population morbidity per 10,000 population there are 1268 diseases of the circulatory system which are as follows: structures of the cardiovascular system are 47.6 percent, hypertension is 21.8 percent, cerebrovascular disease is 13.8 percent, lymphatic and nodular diseases are 6.2 percent, rheumatic heart disease is 1.7 percent, arterial, arteriolar and capillary diseases are 1.2 percent, and venous and other diseases of the cardiovascular system account for 7.7 percent [1].

The World Health Organization (WHO) African region has

the highest prevalence of high blood pressure at 27 %, while the WHO Americas has the lowest prevalence of high blood pressure at 18 %. Hypertension, or elevated blood pressure, is a serious medical condition that significantly increases the risk of heart, brain, kidney, and other diseases. Hypertension may be defined by using specific systolic and diastolic blood pressure levels or the reported use of antihypertensive drugs. An estimated 1.4 billion people worldwide have high blood pressure, but just 14 % have it under control [2].

Owing to the global impact of hypertension, many studies have investigated antihypertensive medications and new therapeutic alternatives [3, 4]. The pathophysiology of hypertension involves the impairment of renal pressure natriuresis, the feedback system in which high blood pressure induces an increase in sodium and water excretion by the kidney that leads to a reduction of the blood pressure. Pressure natriuresis can result from an impaired renal function, inappropriate activation of hormones that regulate salt and water excretion by the kidney (such as those in the renin-angiotensin-aldosterone system), or excessive activation of the sympathetic nervous system [5].

Panzeria alaschanica Kupr is a perennial herbaceous plant of the family Labiate and is distributed primarily in the Ordos, Alasha area of Inner Mongolia, China. It is used as a remedy for postpartum abdominal pain, irregular menstruation, and dysmenorrhea due to its effects on menstruation and blood circulation [6, 7]. It is widely used in Mongolia as a substitute for Leonurus artemisia, which is used in the treatment of irregular menstruation, dysmenorrhea, amenorrhea, endless lochia, and acute nephritis edema. However, there are few reported phytochemistry studies [8 - 10] to support these claimed therapeutic and medicinal effects. Recently, a systematic chemical study conducted on the aerial parts of the plant Panzeria alaschanica Kupr resulted in the isolation of two new acylated flavone glycosides known phenylethanoid [11 - 14].

A recent study of Wang et al. demonstrated two new flavone C-glycosides, named panzeroside A and B which were isolated from the butanolic extract of the aerial parts of Panzeria alaschanica Kupr. Further, anti-inflammatory and analgesic activities were assessed in rats and revealed that these two compounds had significant and dose-dependent analgesic and anti-inflammatory effects [15]. Another study of in vivo antioxidative potential of 5, 7, 4›-trihydroxyflavone-7-O-(6″-O-[E]-coumaroyl)-β-glucopyranoside (TFGN) isolated from Panzeria alaschanica in a diabetic rat model showed that the level of MDA in plasma was reduced to the same level as in healthy control animals. A significant decrease was observed in the plasma α-tocopherol level in the oxidative stress group compared to the healthy controls [16]. Bao et al. discovered that stachydrin hydrochloride, an alkaloid component identified in Panzeria alaschanica Kupr, exhibited potent anti-tumor activity in breast cancer. In the method, molecular docking combined with cellular thermal shift assay (CETSA) was used for analysis [17].

According to the results of the previous study, the species of Panzeria alaschanica are able to reduce the area of anti-inflammatory activity. However, particularly, anti-hypertensive effects of Panzeria alaschanica Kupr has not been studied yet. Therefore, the main purpose of this research was to investigate the regulation of hypertension by Panzeria alaschanica Kupr at low, medium, and high doses (32, 64, 160 mg/kg) and at different time points such as 5, 8, 13, and 15 days after oral gavage, and its renin, angiotensin, and aldosterone effect on the system, stressed by the reduction of sodium reabsorption, to determine the anti-inflammatory effect by inhibiting the production of acute inflammatory secretions related to arterial pressure.

Materials and Methods

Research design

All animals were divided randomly into healthy non-treated controls and an experimental group for the arterial pressure reduction. The group that created the pathological model is considered the control group and was given Dexamethasone. A comparative study group with an experimental group is a comparison group. Captopril was chosen for the experiment because it belongs to the angiotensin-converting enzyme inhibitor group. This medicine is registration code C09AA01 in the international drug classification system.

The effect of the plant *Panzeria alaschanica Kupr* on mean aterial pressure and systolic as well as diastolic pressure was measured on the 5th, 8th, 13th and 15th days of the experiment. Additionally, the effects of the plant *Panzeria alaschanica Kupr* on serum renin, aldosterone and angiotensin II (ANG2) were measured at once on the 15th day.

An extract of Panzeria alaschanica Kupr for a 1:10

infusion was prepared by placing 10 g dry substance in a 250 ml glass beaker in accordance with the Mongolian National Pharmacopoeia, and adding 100 ml of cold distilled water, then putting it in a boiling water bath to brew for 15 minutes, and allowing it to cool to room temperature for 45 minutes. Then, two layers of gauze were placed in a funnel tube and the mixture was filtered into a dimensional cylinder. The remaining slag was gently squeezed. Distilled water was added to make 100 ml total volume.

Plant material and extraction of *Panzeria alaschanica Kupr*

Panzeria alaschanica Kupr, used in the study, was collected from the upper part of *Panzeria alaschanica* Kupr, which grows in Ordos, Alasha, Inner Mongolia, and the Southern Gobi region of Mongolia, and is used in summer by drying.

Experimental animal

The experiment used 60 relatively healthy Wistar rats weighing 150 - 250 grams and 20 laboratory white mice weighing 20 - 33 grams, bred in the Vivar at the Institute of Traditional Medicine and Technology. During the experiment, the animals had access to food and water and were maintained at 20 ± 2° C with a 12 h light/dark cycle.

The study was conducted at the Pathology Laboratory of the International School of Mongolian Medicine of the National University of Medical Sciences, the Research Center of the Institute of Traditional Medicine and Technology, the National University of Inner Mongolia, and the Mongolian-Chinese Hospital in Baotou, and the Veterinary Institute.

Toxicological study methodology

The toxicology was measured by the method of Prozorovskii (1978) [17]. A total of 20 laboratory white mice were selected for the experiment and observed for 72 hours by injecting Panzeria alaschanica Kupr into the abdomen, the lethal dose was determined by Sidorov [18] and the active dose were determined by Zapadnyuk [19].

Study of the plant *Panzeria alaschanica* Kupr arterial pressure lowering mechanism methodology

The experiment was performed using Sharon Leng Hong Ong (2009) [20], a male rat weighing 150 - 250 grams. In the control, comparison, and experimental groups I, II, and III, dexamethasone 20 mcg/kg was injected subcutaneously for 14 days, in the captopril comparator group at 60 mg/kg, and in the experimental group, Panzeria alaschanica Kupr plant extract was taken orally for 15 days from the date of inoculation in small, medium, and large doses.

On days 5, 8, 13, and 15 of the experiment, body weight, ECG, heart rate, and blood pressure were measured in the tail of the rats using a neurological systolic instrument 1.2.

At the end of the experiment, the animals were anesthetized with a dose of 90 mg/kg of ketamine hydrochloride, a heart puncture was performed, a blood sample was taken, and the plasma was separated by a 3000 rpm centrifuge for 15 minutes. The amount of renin, angiotensin II and aldosterone were determined by enzyme-linked immunosorbent assay.

Experimental groups: Healthy group - Kept under normal conditions; Control group - Dexamethasone 20 μg/kg; Comparison group - Dexamethasone 20 μg/kg + Captopril (100 mg/kg); Experimental group I - Dexamethasone 20 μg/kg + Panzeria alaschanica Kupr (32 mg/kg); Experimental group II - Dexamethasone 20 μg/kg + Panzeria alaschanica Kupr (64 mg/kg); Experimental group III - Dexamethasone 20 μg/kg + Panzeria alaschanica Kupr (160 mg/kg).

Statistical analysis

We expressed continuous variables including systolic and diastolic blood pressure, aldosterone and angiotensin II as the mean and standard deviation. The main effects of arterial pressure, Panzeria alaschanica preparation and their interaction were determined using a mixed two - way ANOVA with a Greenhouse-Geiser adjustment for lack of sphericity. The repeated measurements within subjects were then compared to the previous time interval using paired t-tests. A Bonferroni-type correction was applied to all test results resulting in a significance level set at $p < 0.05$. Comparing the mean of the continuous variables between groups, one-way ANOVA was carried out, and followed the Tukey test as multiple comparison. Statistical analysis was performed using STATA 14.0 software.

Ethical statement

The animal study was carried out in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals (NIH Publications No. 80-23) revised in 1996. Formal

approval to conduct the experiments was obtained from the Ethical Committee of the Mongolian National University of Medical Sciences (Protocol No.2018 / 3-18). All efforts were made to minimize the number of animals used and their suffering.

Results

Results for the determination of the toxicological (LD_{50}) of the *Panzeria alaschanica* Kupr

In the toxicological study, LD_{50} of *Panzeria alaschanica* Kupr extract was found to be LD_{50} = 1.6 (1.4 - 1.9) g/kg by Prozorovskii (1978) express method. In toxicological according to Sidorov's (1973) classification, the acute dose was ED = 32 (16-200) mg/kg by Zapadnyuk.

Effects of *Panzeria alaschanica* Kupr on the pathogenesis of arterial hypertension caused by dexamethasone in rats

Dexamethasone is used for the treatment of inflammatory diseases, such as asthma, as well as respiratory and immune diseases. Dexamethasone is a synthetic glucocorticoid that induces fibrosis with impaired heart rate, body mass ratio, and left ventricular dysfunction. Dexamethasone has immunosuppressive and anti-inflammatory effects.

The mean arterial pressure in the healthy group was 17.8 % on the 5th day, 55.3 % on the 8th day, and 77.8 % on the 13th day, compared to the control group. On the 15th day, an increase of 49.2 % was observed, indicating a pathological pattern of arterial hypertension under the influence of dexamethasone. As shown in Table 1, Panzeria alaschanica Kupr, at a dose of 32

Table 1. The effect of the plant Panzeria alaschanica Kupr on mean arterial pressure.

Days	Healthy - 3 (n = 19)	Control - 2 (n = 28)	Captopril-1[a] (n = 22)	Kupr32 - 5 (n = 26)	Kupr64-6 [b, c] (n = 28)	Kupr160 -4 (n = 28)		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	F	p-value
5 day	76 ± 15.4	89.5 ± 13.5	11.7 ± 16.6	92.0 ± 20.2	88.4 ± 13.5	76.9 ± 12.4	1.836	0.103
8 day	85.6 ± 16.8	132.9 ± 12.4	101.1 ± 7.2	84.6 ± 24.3	109.6 ± 25.5	89.3 ± 19.4	6.404	0.071
13 day	90.2 ± 24.9	160.4 ± 26.7	84.0 ± 10.1	77.3 ± 10.8	80.5 ± 13.4	81.6 ± 17.9	1.315	0.184
15 day [d]	88.2 ± 16.4	131.6 ± 25.1	113.0 ± 19.6	74.9 ± 18.4	76.7 ± 10.2	112.6 ± 14.8	7.147	0.001

The mixed two-way ANOVA results: interaction of arterial pressure and effect of Panzeria alaschanica Kupr preparation F(1.621, 195.61) = 17.109, p < 0.054; Main effect of arterial pressure F (1.831, 485.49) = 284.14, p < 0.014; Main effect of Panzeria alaschanica preparation F(1,161) = 0.847, p = 0.158; Pairwise comparisons: [a]5 day vs. 15 day, p = 0.051; [b]5 day vs. 15 day, p = 0.031; [c]8 day vs. 15 day, p=0.014; Multiple comparisons: [d]Captopril-1 vs. Kupr64-6, p = 0.000.

Table 2. The effects of the plant Panzeria alaschanica Kupr on arterial systolic blood pressure.

Days	Healthy-3 (n = 19)	Control -2 (n = 28)	Captopril-1 [a, b] (n = 22)	Kupr32-5 (n = 26)	Kupr64-6 [c, d] (n = 28)	Kupr160 - 4 (n = 28)		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	F	p-value
5 day	87.8 ± 18.4	107.4 ± 10.3	124.0 ± 12.2	115.4 ± 23.5	108.6 ± 12.1	90.4 ± 13.7	0.076	0.413
8 day	97.6 ± 14.6	146.4 ± 9.6	117 ± 2.0	98.4 ± 28.6	132.6 ± 25.0	104.2 ± 18.3	7.300	0.058
13 day	105.8 ± 28.8	178.4 ± 30.3	98.0 ± 9.9	85.0 ± 4.5	96.2 ± 11.7	95.6 ± 19.0	5.149	0.084
15 day [e]	106.2 ± 18.6	151.4 ± 25.4	127.2 ± 22.7	91.6 ± 21.8	95.8 ± 14.1	128.6 ± 15.1	6.150	0.051

The mixed two-way ANOVA results: interaction of arterial pressure and effect of Panzeria alaschanica Kupr preparation F (1.132, 682.14) = 26.151, p < 0.005; Main effect of arterial pressure F (1.331, 567.142) = 362.82, p < 0.014; Main effect of Panzeria alaschanica preparation F (1,619 = 0.564, p = 0.345; Pairwise comparisons: [a]8 day vs. 15 day, p = 0.001; [b]8 day vs. 13 day, p = 0.014; [c]8 day vs. 13 day, p=0.031; [d]13 day vs. 15 day, p=0.000; Multiple comparisons: [e]Captopril-1 vs. Kupr64-6, p = 0.001.

Table 3. The effects of the plant Panzeria alaschanica Kupr on arterial diastolic blood pressure.

	Healthy-3 (n = 19)	Control-2 (n = 28)	Captopril-1[a, b] (n = 22)	Kupr32-5 (n = 26)	Kupr64-6[c, d] (n = 28)	Kupr160-4 (n = 28)		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	F	p-value
5 day	64.2 ± 12.3	71.6 ± 16.6	99.4 ± 20.9	68.6 ± 16.8	68.2 ± 14.9	63.4 ± 11.0	1.145	0.630
8 day	73.6 ± 19.0	119.4 ± 15.1	85.2 ± 12.3	70.8 ± 19.9	86.6 ± 26.0	74.4 ± 20.5	4.451	0.061
13 day	74.5 ± 21.0	142.4 ± 23.1	70.0 ± 10.3	69.6 ± 17.1	64.8 ± 15.1	67.6 ± 16.8	1.458	0.091
15 day[e]	70.2 ± 14.2	111.7 ± 24.7	98.8 ± 16.5	58.2 ± 15.0	57.6 ± 6.2	96.6 ± 14.5	6.691	0.050

The mixed two-way ANOVA results: interaction of arterial pressure and effect of Panzeria alaschanica Kupr preparation F (1.731, 754.11) = 14.284, p < 0.051; Main effect of arterial pressure F (1.414, 549.421) = 387.14, p < 0.021; Main effect of Panzeria alaschanica preparation F (1.841, 742.48) = 13.564, p = 0.345; Pairwise comparisons: [a]8 day vs. 13 day, p = 0.000; [b]8 day vs. 15 day, p = 0.001; [c]8 day vs. 13 day, p=0.003; [d]13 day vs. 15 day, p=0.003; Multiple comparisons: [e]Captopril-1 vs. Kupr64-6, p = 0.053.

Table 4. Effects of the plant Panzeria alaschanica Kupr on rat serum renin, aldosterone, and angiotensin II (ANG2).

Variables	Healthy-3 (n = 19)	Control-2 (n = 28)	Captopril-1 (n = 22)	Kupr32-5 (n = 26)	Kupr64-6 (n = 28)	Kupr160-4 (n = 28)		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	F	*p-value
Renin[a, b, c]	139.2 ± 6.01	231.2 ± 85.5	140.8 ± 9.3	147.0 ± 16.2	148.7 ± 18.5	146.0 ± 31.1	7.123	0.010
Aldosterone[d, e, f]	3.28 ± 0.42	5.90 ± 2.35	3.41 ± 0.73	3.33 ± 0.63	3.56 ± 1.08	3.40 ± 0.42	6.491	0.050
Angiotensin II	77.2 ± 12.1	103.6 ± 13.9	74.2 ± 9.57	80.1 ± 12.1	68.0 ± 12.2	72.5 ± 5.67	5.481	0.071

*One-way ANOVA; Multiple comparisons: [a]Control-2 vs. Kupr32-5, p = 0.001; [b]Control-2 vs. Kupr64-6, p = 0.000; [c]Kupr32-5 vs. Kupr64-6, p = 0.002; [d]Control-2 vs. Captopril-1, p = 0.014; [e]Captopril-1 vs. Kupr32-5, p = 0.006; [f]Control-2 vs. Kupr64-6, p = 0.004.

mg/kg, tesulted in a mean blood pressure of 36.3 % from day 8 compared with controls; by the 13th day it was 51.8 %. On the 15th day, it decreased by 43.1 % (p < 0.05) (Table 1).

In addition, the mean blood pressure was 17.5 % from the 8th day for animals receiving Panzeria alaschanica Kupr at a dose of 64 mg/kg compared to the animals of the control group; on the 13th day it was 49.8 %. On day15 it fell by 41.7 % respectively (p < 0.05).

Figure 1 shows that the average effect of the plant Panzeria alaschanica Kupr on the pathogenic model of dexamethasone-induced high blood pressure was halved on the 13th days of the experiment, with a statistically significant difference compared with the pathogenic control group. On the 13th days of the experiment, the animals in the comparative group had a

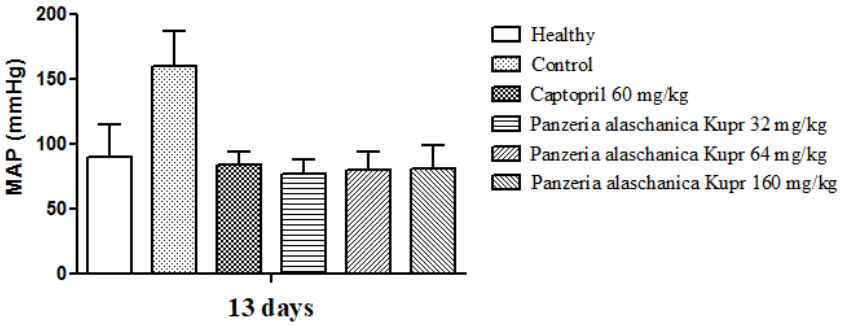

Figure 1. Effect of the plant Panzeria alaschanica Kupr on mean arterial pressure.

decreased blood pressure by a statistically significant difference of 47.6 % compared to the control group (Figure 1).

Dexamethasone increased systolic blood pressure by 22.3 % on the 5th day compared with controls in healthy groups of animals with arterial hypertension by 50 % on the 8th day; by 68.6 % on the 13th , and by the 15th day a statistically significant increase of 42.6 %, respectively, indicating the presence of a pathological pattern. Systolic blood pressure increased by 20 % starting on the 8th day compared to control animals (captopril dose 60 mg/kg) compared to control groups animals on the 13th day, and it decreased by 45 % ($p < 0.05$) respectively.

When the plant Panzeria alaschanica Kupr was administered at a dose of 32 mg/kg, systolic blood pressure increased by 7.4 % on the 5th day compared to the control group, at 64 mg/kg it decreased by 1.1 % compared to the control group, and at a dose of 160 mg/kg it decreased by 15.8 %. In the plant Panzeria alaschanica Kupr group at a dose of 32 mg/kg, systolic blood pressure was 32.8 %, over the 8 days, at the dose of 64 mg/kg it was 9.4 %, and at the dose of 160 mg/kg it was 28.8 %. In comparison to controls it had declined.

However, in the Panzeria alaschanica Kupr factory at a dose of 32 mg/kg, systolic blood pressure rose by 39.4 % on the 15th day compared to the control group, a decrease of 36.7 % to the dose of 64 mg/kg and 15 % to a dose of 160 mg/kg was observed (Table 2).

Systolic blood pressure in the Panzeria alaschanica Kupr group at a dose of 32 mg/kg compared to controls was 52.4 % on the 13th day, and systolic blood pressure rose 46.1 % from the 13th day compared to the control group at a dose of 64 mg/kg. Compared to the control group in animals dosed with 160 mg/kg, systolic blood pressure was reduced by 46.4 % ($p<0.05$) (Figure 2).

Table 3 shows a statistically significant increase in diastolic blood pressure in the health group of 11.5 % on the 5th day; 62.2 % on the 8th day; 91.1 % on the 13th day, and 59.1 % on the 15th day versus the pathogen experimental group. Panzeria alaschanica Kupr was compared to the control group at a dose of 32 mg/kg diastolic arterial pressure, which has increased 40.7 % since the 8th day. On the 15th day, it declined by 47.9 % ($p < 0.05$) respectively. In addition, animals who received Panzeria alaschanica Kupr in comparison with the animals in the control group had an increased diastolic blood pressure by 27.5 % from the 8th day to the 15th day, and it fell by 48.4 % ($p < 0.05$) respectively.

Diastolic blood pressure increased 37.7 % from the 8th day of Panzeria alaschanica Kupr at a dose of 160 mg/kg compared to controls; On day 15, it decreased by 13.5 % ($p < 0.05$) respectively.

The arterial diastolic blood pressure increased by 28.6 % from the 8th day compared with the animals in the control group given Captopril a dose of 60 mg/kg; On the 15th day, a statistically significant difference ($p < 0.05$) was decreased by 11.5 % respectively (Table 3).

However, the effect of Panzeria alaschanica Kupr on dexamethasone-induced hypertension was found to be a statistically significant reduction in diastolic blood pressure during the 13 days of the comparison with the control group in the pathogen model. On the 13 days of the experiment, the animals in the comparative group decreased by a statistically significant difference of 50.8 % compared to the control group

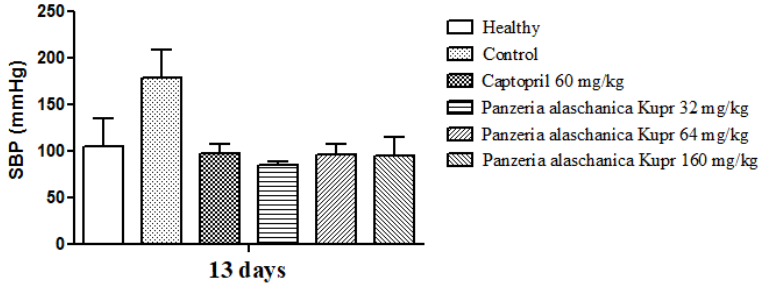

Figure 2. Effect of the plant Panzeria alaschanica Kupr on systolic pressure.

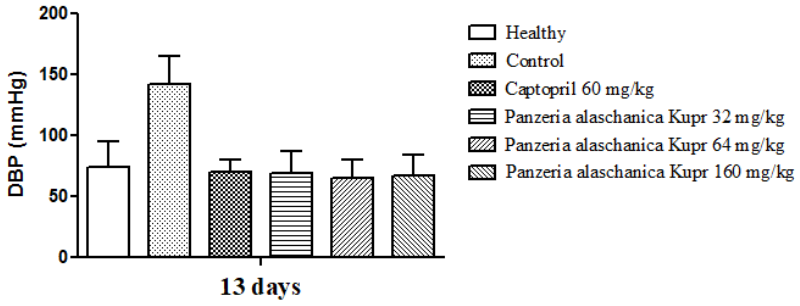

Figure 3. Effect of the plant Panzeria alaschanica Kupr on arterial diastolic pressure.

(Figure 3).

Dexamethasone was used to model the pathogenesis of high blood pressure and to determine the activity of enzymes such as renin, aldosterone, and angiotensin in the blood plasma of experimental animals. The renin rate (231.2 ± 85.5) in the control group was 66 % higher than in the healthy group (139.2 ± 6.01), 79.8% of the aldosterone rates (5.90 ± 2.35), the amount of angiotensin II (103.6 ± 13.9) of 34.1% resulted in a statistically significant difference, which was a pathological profile or an increase in blood pressure ($p < 0.05$) (Table 4).

The pathological pattern as determined by the level of renin (140.8 ± 9.31) in the blood of comparable animals was 39.1 % compared to the control group (231.2 ± 85.5), and the aldosterone control group (3.41 ± 0.73) was 42.2 % relative to the control group (5.90 ± 2.35), resulting in a pathological profile. The angiotensin II enzymatic activity reduction group (74.2 ± 9.57) was reduced by a statistically significant deviation ($p < 0.05$) of 28.4 % from the control group (103.6 ± 13.9) (Figure 4).

Based on the study findings, the experimental group which ingested a dose of 160 mg/kg of plant Panzeria alaschanica Kupr, resulted in a renin level of 36.8 % compared to the control group (231.2 ± 85.5) that caused the pathological model. The amount of aldosterone in Panzeria alaschanica Kupr animals that ingested a dose of 32 mg/kg was 43.5 % of the animals ingested (3.33 ± 0.63) compared to the pathogen group (5.90 ± 2.35). The amount of angiotensin II in animals which ingested Panzeria alaschanica Kupr at dose of 64 mg/kg (68.0 ± 12.2), was reduced by a statistically significant difference ($p < 0.05$) of 34.3 % from the control group (103.6 ± 13.9) which produced the pathological model (Figure 5, 6).

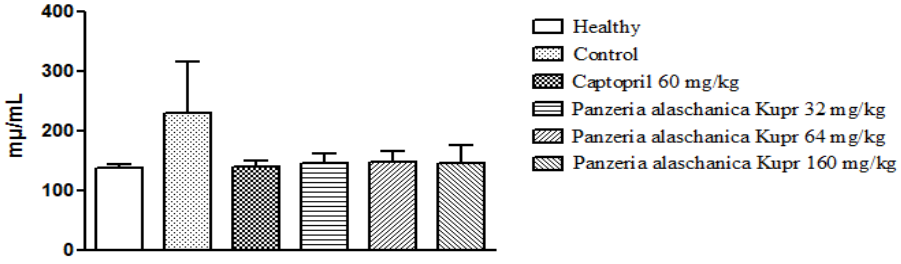

Figure 4. Effects of Renin on the plasma of Panzeria alaschanica Kupr plant.

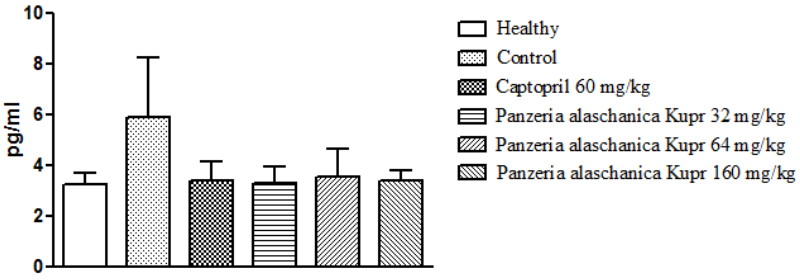

Figure 5. Effects of aldosterone on blood plasma of Panzeria alaschanica Kupr plant.

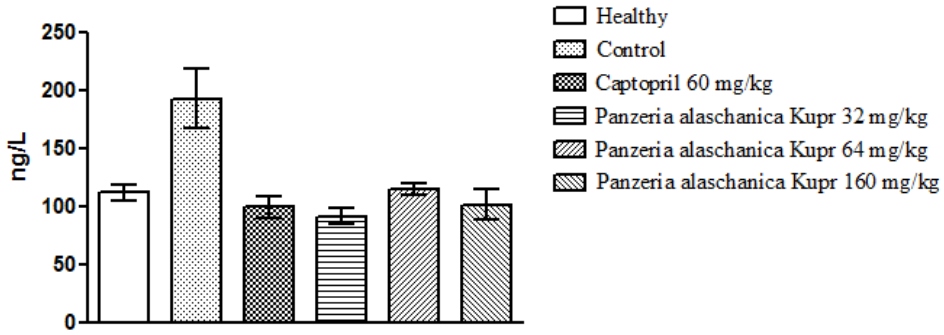

Figure 6. Effect of angiotensin II on the blood plasma of Panzeria alaschanica Kupr plant.

Discussion

Arterial hypertension is one of the most common non-communicable diseases. This is due to its the high prevalence in the population, the high risk of complications, the lack of control, and the influence of social factors. In our country, 50.0 % of cardiovascular diseases are the leading cause of death in the population, at 503.9 per 10,000 population. It accounts for 1.3 % of deaths. According to international guidelines, arterial hypertension is defined as a systolic pressure of 140 mm Hg or more and a diastolic pressure of 90 mm Hg or more after several (4 - 6) measurements. Arterial hypertension is divided into two groups according to its cause: primary and secondary. Primary hypertension is 85 - 90 % of total hypertension and secondary hypertension is 10 - 15 % [20, 21]. Recently, the comorbidities associated with hypertension have made it harder to control blood pressure. According to 2017 ACC/AHA guidelines, 16 % of hypertensive patients suffered from chronic kidney disease [22]. Meanwhile, the guidelines recommended that angiotensin-converting enzyme inhibitors should be used in hypertension and chronic kidney disease patients [23].

The Panzeria alaschanica Kurp contains essential oils, iridoids (harpings), kaempferol flavonoids, quercetin, isorhamnetin, preservatives, organic and phenolic carboxylic acids (chlorogenic, neochlorogens, caffeinated acids), malic acid, alkaloids, and ascorbic acid. Wang et al. found that the use of Panzeria alaschanica had an impact on egg albumin- and carrageenan-induced anti-inflammatory drugs in rats. A systematic chemical study was carried out on the EtOAc extract of Panzeria alaschanica, which led to the isolation of phenylpropanoids and flavonoids from the plant for the first time [15]. In the present study, we confirmed that when Panzeria alaschanica Kupr was administered at a dose of 32 mg/kg, for 15 days, arterial pressure was decreased by 23.7 % ($p < 0.05$), while at the dose of 64 mg/kg, on the 15 days, it decreased by 43.1 % ($p < 0.05$). The mean arterial pressure in the healthy group was 17.8 % on the 5th day compared to the control group; 55.3 % on the 8th day; 77.8 % on the 13th day; and on the 15th

day, an increase of 49.2 % was observed, indicating a pattern of arterial hypertension under the influence of dexamethasone. Owing to the global impact of hypertension, many studies have investigated antihypertensive medications and new therapeutic alternatives. Dignesh et al. demonstrated that animals treated with dexamethasone along with beta Vulgaris (a dose of 100 and 300 mg/kg for 14 days) showed a significant ($p < 0.05$) decreased heart rate in comparison with the dexamethasone group [20]. Further, in our study, systolic blood pressure increased by 50 % from the 8th day of the comparable group (captopril a dose of 60 mg/kg) relative to the control group; on the 13th day, it decreased by 68.6 % ($p<0.05$) respectively. Captopril, as an enzymatic angiotensin-converting inhibitor, has been widely used for the treatment of high blood pressure and cardiovascular disease [24]. Further, at a dose of 32 mg/kg, systolic blood pressure was 32.8 %, over the 8 days, the dose of 64 mg/kg was 9.4 %, and 160 mg/kg at 28.8 % in comparison to controls had declined. To confirm the study results, the activity of enzymes such as renin, aldosterone, and angiotensin II in the blood plasma of experimental animals was determined in 66 % of the control animals with respect to the healthy group, 79.8 % with respect to aldosterone, and 34.1 % with respect to angiotensin II. This led to a statistically significant increased finding of a pathological pattern or an increase in blood pressure ($p < 0.05$). Jung et al. showed that the ethanolic extract of A. sessiliflorus fruit demonstrated free radical scavenging capacity, enhanced endothelial nitric oxide (NO) production, and inhibited angiotensin-converting enzyme (ACE) activity in spontaneously hypertensive rats (SHRs), resulting in the improvement of vascular relaxation and decrease in blood pressure in the hypertensive animal model [25, 26]. Administration of Phragmanthera incana leaf ethanol extract dose-dependently and significantly reduced systolic blood pressure and mean arterial pressure in hypertensive rats. The extract significantly ($p < 0.05$) reversed elevated IL-6 and TNF-α in hypertensive rats and demonstrated antioxidant activity by attenuating L-NAME-induced elevated malondialdehyde and depletion of reduced glutathione and catalase activity in rat tissues [26].

The limitation of this study is that we did not confirm how Panzeria alaschanica Kupr influenced the expression and production of the anti-inflammatory cytokine related to the high blood pressure expression and production. Therefore, future studies need to be done to determine the effect of the plant Panzeria alaschanica Kupr on blood serum and brain tissue levels of TNF-α, IL-6, IL-1β, and IL-10. Also, brain tissue levels of TGF-β, BDNF, TrkB, and NGF need to be determined by real-time polymerase chain reaction.

Conclusion

In summary, it has been demonstrated that Panzeria alaschanica Kupr reduces high blood pressure. Pathogenesis has been shown to induce peripheral vasoconstriction with increased release of aldosterone by angiotensin conversion enzymes. Panzeria alaschanica Kupr reduces the effects of vasoconstriction and hypertension by reducing the release of renin and aldosterone. The results will be used to study the mechanisms of blood pressure reduction in Panzeria alaschanica Kupr, which may allow us to develop a new therapeutic approach to prevent and treat arterial hypertension.

Conflict of Interest

The authors state no conflict of interest.

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