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ORIGINAL RESEARCH

Impact of tannic acid on blood pressure, oxidative stress and urinary parameters in L-NNA-induced hypertensive rats

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Abstract Hypertension is a major health problem with increasing prevalence around the world. Tannic acid is water-soluble polyphenol that is present in tea, green tea, coffee, red wine, nuts, fruits and many plant foods. It has been reported to serve as an antioxidant or a pro-oxidant depending on the type of cells and its concentration. The purpose of our study was to evaluate the effect of tannic acid on systolic blood pressure, oxidative stress and some urinary parameters in the rat model of essential hypertension. Blood pressures of all rats were measured using the tail-cuff method. The nitric oxide synthase inhibitor N (omega)-nitro-L-arginine was administered orally at a dose of 0.5 g/l/day for 15 days to rats in order to create an animal model of hypertension. Tannic acid was intraperitoneally injected at a dose of 50 mg/kg for 15 days. Superoxide dismutase, catalase activity and the concentration of malondialdehyde (MDA) were determined in blood plasma and homogenates of heart, liver and kidney. In order to evaluate renal functions, urine pH, urine volume, urine creatine, uric acid, and urea nitrogen values were measured. Compared with the hypertension group, a decrease in MDA concentrations of heart tissue ($p < 0.01$), urea nitrogen values ($p < 0.01$) and urine volumes ($p < 0.001$) were established in hypertension + tannic acid group. There was also a decrease in blood pressure values (20th and 30th days) of this group, but there was no a statistical difference according to hypertension group. The findings of our research show the effect of tannic acid in lowering blood pressure in hypertensive rats.

Keywords Hypertension · Tannic acid · Systolic blood pressure · Oxidative stress · Urinary parameters

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Introduction

Hypertension (HT) is a significant health issue with a gradually increasing prevalence. It was reported to have affected 972 million people around the world and to have a prevalence of 26.4 % in the year 2000. It is foreseen to have a prevalence of 29.2 % by 2025 and to affect 1 billion 56 million people (Kearney et al. 2005). HT is an important risk factor for stroke, myocardial infarction, cardiac and renal failure. HT is predicted to cause 7.1 million early deaths around the world. According to data of the World Health

Organization collected in 2000, HT ranks first among the preventable deaths in the world (World Health Organization 2003).

Reactive oxygen species (ROS) that contain an unpaired electron in the final orbit of their atomic structures, highly reactive, and are endogenously synthesized side products. If not immediately detoxified where they are synthesized, ROS can cause numerous diseases including hypertension. ROS were shown to stimulate the growth and proliferation of vein smooth muscle cells (Ruiz-Gutierrez et al. 2001; Kour and Perkins 1991).

Substances that prevent or postpone the oxidation of substances that can be oxidized such as protein, lipid, carbohydrates, and DNA found in live cells are called antioxidants, and such reactions carried out by antioxidants are defined as antioxidant defense. This system demonstrates itself by preventing excessive production of free radicals or by reducing or repairing the damage. These systems contain such endogenous enzymes as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) (Ozbayer et al. 2011).

Oxidative stress level increases in hypertension and in relation to that, reactive oxygen species release shows a rise. Increase in malondialdehyde (MDA) that is the final product of lipid peroxidation which causes oxidative stress is another physiological characteristic of hypertension. High ROS amount inhibits the activity of antioxidants such as SOD and CAT and decreases the antioxidant capacity. In a study that compared the blood samples of essential hypertensive patients and normotensive individuals, high level of MDA concentration was established, and in addition, the presence of low SOD activity was also shown (Russo et al. 1998). This demonstrates that oxidative stress plays an important role in the pathogenesis of essential hypertension.

Fruits and vegetables rich in polyphenol, and drinks such as tea and wine, act as inhibitors and are protective for various human cancers and cardiovascular diseases (Gulcin et al. 2010). Tannins found in such food are divided into two classes as hydrolyzed and condensed tannins (Labieniec and Gabryelak 2006; Cowan 1999; Cosan et al. 2011). Polyphenols containing tannin possess biological activities as antitumor, antiviral, anti-HIV, lipid peroxidation inhibition, and plasmin activity (Labieniec and Gabryelak 2003; Cosan et al. 2010). Among the hydrolyzed tannins, tannic acid, is found in green tea, coffee, red wine, such nuts as hazelnuts and walnuts, fruits, and most plants (Cowan 1999; Taffetani et al. 2005; Marienfeld et al. 2003; Cosan et al. 2009). Tannic acid has major biological activities such as anticarcinogenic, antioxidant, antimutagenic, antimicrobial, antiallergic, antiinflammatory, and stopping bleeding (Labieniec and Gabryelak 2006; Cowan 1999; Marienfeld et al. 2003). In addition, tannic acid can serve as antioxidant or prooxidant depending on the cell type used and its concentration (Labieniec and Gabryelak 2003). Polyphenols are also known to have an antihypertensive effect (Rodrigo et al. 2012).

Along with the discovery of nitric oxide (NO) in 1980s, researches were focused on the correlation of blood pressure increase with the reduction in NO synthesis. NO is synthesized by nitric oxide synthase (NOS) enzymes from L-arginine. A hypertension model was developed that is based on the increase in arterial blood pressure as a result of chronic inhibition of NOS enzymes with such L-arginine analogues as NG-nitro-L-Arginine (L-NNA), and NG-nitro-L-arginine methyl ester (L-NAME) (Ribeiro et al. 1992). Chronic NOS inhibition is commonly used in essential hypertension research. Chronic NOS inhibition of total peripheral resistance increase, increased renal sodium involvement, sympathetic system activation, and various vasoactive substances is accepted to provide mediated hypertension (Zatz and Baylis 1998).

The aim of this study is to investigate the effects of tannic acid on antioxidant system and renal functions disrupted by hypertension, increased free radicals, and blood pressure. Thus, the effects of tannic acid in essential hypertension model on systolic blood pressure and values of SOD, MDA, and CAT in blood, heart, liver, and renal tissues were investigated. In order to evaluate the effect of tannic acid on renal functions, urine pH, urine volume, urine creatine, uric acid, and urea nitrogen values were measured.

Materials and method

Twenty eight female Spraque–Dawley rats of 250–300 g weight and aged 4–5 months were used in the experiment. Rats were placed in special cages in groups of seven and were applied care under standard conditions (12 h of daylight, 12 h of dark, ventilated, fixed temperature rooms). Standard rat pellet food of

8 mm was given to rats for nourishment and tap water was provided as drinking water. Weight increases of the subjects were measured with an electronic scale (Chyo MP-300 electronic balance, Chyo Balance Corp, Kyoto, Japan) at the beginning and in the end of experiment. Approval was obtained for our study from the Experimental Animals Local Ethics Committee of Eskisehir Osmangazi University (Ethics Committee Ref No: 188/2011).

Rats were divided into four experimental groups with seven rats in each group. Substances administered to experimental groups, duration, and amounts are given in Table 1.

Daily L-NNA and tannic acid amounts to be administered to rats were estimated according to planned concentrations (Ribeiro et al. 1992; Krajka-Kuzniak et al. 2008). A study by Ribeiro et al. (1992) that defined first the experimental hypertension model with chronic nitric oxide synthase inhibition was taken as reference and L-NNA was administered to rats. Systolic blood pressure measurements were carried out from the tail by the indirect "tail-cuff" method (MAY BPHR 9610-PC tail-cuff indirect blood pressure recorder, Commat Ltd., Ankara, Turkey) without the use of anesthetics on the day before the administration of L-NNA and on the 15th, 20th, and 30th days following the beginning of the experiment. After blood pressure measurements were conducted on the 30th day, rats were taken to urine collection cages labeled based on groups and their 18-h urine samples were obtained. Following the determination of volumes of collected urine samples, pH values of each sample were measured with a pH meter (inoLab pH 720, WTW Laboratory, Weilheim, Germany). Other urine parameters were analyzed spectrophotometrically. After the urine collection process, rats were put to sleep with ether anesthesia and approximately 2 ml blood sample of each rat was obtained from left ventricle of the heart and put in EDTA tubes. Heart, liver, and kidney tissues were taken and frozen in liquid nitrogen. Following hemoglobin measurement, hemolysates were prepared from blood samples taken to EDTA tubes and homogenates were prepared from frozen heart, liver and kidney tissues, and protocols necessary for SOD, MDA, and CAT measurements are carried out. Erythrocyte hemolysates were prepared by using the method reported by Sun et al. (1988). Blood samples were taken to 2 ml EDTA tubes and plasma and erythrocyte were separated in centrifuge. Erythrocyte pellet left in the tube was washed with 0.9 % NaCl (normal saline) three times and hemolysate was formed. The protocol used by Kiris et al. (2008) was applied for the preparation of tissue homogenates. The prepared hemolysates and homogenates were stored at −80 °C until the measurements of SOD, MDA, and CAT. SOD activity was spectrophotometrically measured with the SOD Determination Kit (Fluka, St. Louis MO, USA, Cat. No: 19160) that is based on WST (water-soluble tetrazolium salt) reaction. Enzyme activity of the samples was established with ELISA at 450 nm by the inhibition of formazan dye based on xantin–xantin oxidase enzymatic method that produces superoxide radicals. The results were put in their respective places in SOD inhibi tion % = $\{[(A_{blank1} - A_{blank3}) - (A_{sample} - A_{blank2})]/(A_{blank1} - A_{blank3})\}$ formula and was expressed as % inhibition (A_{blank1}, A_{blank2}, and A_{blank3} are the absorbance values of standard solutions that are prepared with the kit; A_{sample} is the absorbance value of the sample solution). CAT activity was established by spectrophotometric evaluation of hydrogen peroxide that formed a stable complex with ammonium molybdate (Goth 1991). Absorbance values of B1 (Blank 1), B2 (Blank 2), B3 (Blank 3) and sample tubes against 405 nm distilled water were measured in spectrophotometer.

Table 1 Substances administered to experimental groups

Groups	Duration	Dose	Administered substances
1. Group (control)	–	0.3 ml/kg intraperitoneally	Physiological saline
2. Group (tannic acid)	Last 15 days (one dose every three days)	50 mg/kg intraperitoneally	Tannic acid
3. Group (hypertension)	The first 15 days (one dose every day)	0.5 g/l (added to drinking water)	L-NNA
4. Group (hypertension + tannic acid)	The first 15 days (one dose every day) + last 15 days (one dose every three days)	0.5 g/l (added to drinking water) + 50 mg/kg intraperitoneally	L-NNA + tannic acid

Then, catalase activity of each samples was determined with the formula CAT activity (kU/L) = $[(Abs_{sample} - Abs_{blank1})/Abs_{blank2} - Abs_{blank3})] \times 271$ (Abs_{blank1}, Abs_{blank2}, and Abs_{blank3} are absorbance values of standard solutions that are prepared according to Goth (1991)). MDA concentration was established according to the method based on color reaction of MDA with thiobarbituric acid (TBA) (Mihara and Uchiyama 1978). Absorbances of blind and sample tubes were read following zeroing with distilled water at 532 nm in spectrophotometer. Defined with nmol/ml, MDA concentration was expressed in nmol/gHb according to hemoglobin (g/dl) value given in "optic densities and hemoglobin g/dl" table by Tanyer for erythrocyte hemolysates (Tanyer 1985).

For urea nitrogen measurement, transformation of urea to ammonium carbonate by degrading it with urease enzyme and its colorimetric measurement of a yellow color formed by Nessler's reagent was taken as the basis (Urease-Nesslerization method). Uric acid amount was established by the colorimetric measurement of the blue color formed by uric acid reducing phosphotungstic acid in mild acidic and sodium carbonate environment (modified Caraway method). The amounts of creatinine in urine samples were measured by the alkaline picrate method (Jaffe's alkaline picrate reaction assay) which is based on the colorimetric measurement using a spectrophotometer of the orange color formed as a result of creatinine transforming picric acid into picramic acid in an alkali environment.

Statistical analysis

The data were summed up as means + SD. Statistical evaluation of the obtained data was carried out with IBM SSPSS for Windows 20.0 software pack. Shapiro–Wilk test was used for establishing the distribution forms of the data. Blood pressure data were assessed with Student's *t*-test and in vitro data were evaluated with one-way ANOVA. In multiple comparisons, Bonferroni test that is among the post hoc tests was used. $p < 0.05$ values were accepted to be statistically significant.

Results

In the 15th day measurements of 3rd and 4th groups, blood pressure values were observed to have increased compared to the control group and the 2nd group. There was a statistically significant difference in this increase ($p < 0.001$). A difference was not observed between the control group and the 2nd group in terms of blood pressure values ($p > 0.05$). It was observed that the 20th day measurement value of the 4th group decreased compared to the 15th day and approached to the control group values. A decrease was established in blood pressure values (20th and 30th days) of rats (4th group) that were administered intraperitoneal tannic acid 15 days after hypertension was created compared to the hypertension group. These values were approaching the control group but a statistical difference was not observed (Table 2).

When compared the hemolysate, heart, and kidney samples between the groups in terms of SOD enzyme activation, no statistical difference was established. However, SOD activation of liver homogenate samples of rats in the 4th group demonstrated a statistically significant drop compared to the 2nd group ($p < 0.05$) (Table 3).

Table 2 Statistical analysis of blood pressure values between the groups

Groups	Blood pressure values (mmHg)			
	1st measurement (0 day)	2nd measurement (15th day)	3rd measurement (20th day)	4th measurement (30th day)
1. Control (n = 7)	122.29 ± 1.11	124.43 ± 1.40	119.86 ± 2.91	119.86 ± 4.81
2. Tannic acid (n = 7)	124.71 ± 2.5	124.86 ± 1.46	123.00 ± 4.97	122.71 ± 4.79
3. Hypertension (n = 7)	127.00 ± 4.62	154.43 ± 10.23**,a	131.43 ± 7.66*,b	134.14 ± 8.32*,b
4. Hypertension + tannic acid (n = 7)	129.71 ± 10.75	145.00 ± 2.77**,a,†	126.43 ± 3.74	128.00 ± 6.95

Each measurement was compared with the other groups at the same measurement time. Compared with the control group ** $p < 0.001$, * $p < 0.01$. Compared with the tannic acid group [a] $p < 0.001$, [b] $p < 0.05$. Compared with the hypertension group [†] $p < 0.05$. The data were summed up as means + SD

Table 3 SOD inhibition values of hemolysate, heart, liver and kidney samples in the experimental groups and their statistical analysis

Groups	SOD inhibition %			
	Hemolysate	Heart	Liver	Kidney
1. Control (n = 7)	71.14 ± 9.30	38.86 ± 9.86	53.00 ± 10.20	50.57 ± 3.87
2. Tannic acid (n = 7)	75.00 ± 10.28	50.00 ± 3.51	63.00 ± 6.53	47.71 ± 10.52
3. Hypertension (n = 7)	78.86 ± 2.97	42.14 ± 11.68	59.71 ± 1.89	47.57 ± 9.00
4. Hypertension + tannic acid (n = 7)	78.71 ± 4.72	45.71 ± 11.40	52.00 ± 8.45[a]	49.86 ± 8.57

Compared with the tannic acid group [a] $p < 0.05$. The data were summed up as means + SD

Table 4 CAT enzyme values of hemolysate, heart, liver and kidney samples in the experimental groups and their statistical analysis

Groups	Catalase			
	Hemolysate (kU/mg Hb)	Heart (kU/ml)	Liver (kU/ml)	Kidney (kU/ml)
1. Control	3.57 ± 0.89	2.23 ± 0.86	2.89 ± 0.90	2.73 ± 1.08
2. Tannic acid	3.98 ± 0.49	0.85 ± 0.41[a]	3.50 ± 0.34	3.17 ± 0.60
3. Hypertension	2.71 ± 0.55[c]	1.44 ± 0.72	3.38 ± 0.33	2.56 ± 0.85
4. Hypertension + tannic acid	2.10 ± 0.38[a,b]	1.44 ± 0.84	3.07 ± 0.22	1.93 ± 0.57[d]

Compared with the control group [a] $p < 0.01$. Compared with the tannic acid group [b] $p < 0.001$, [c] $p < 0.01$, [d] $p < 0.05$. The data were summed up as means + SD

When comparing the CAT enzyme values in the hemolysate samples of the experimental groups, a decrease was established in the 4th group ($p < 0.01$) compared to the control group. When analyzing the CAT enzyme values in the homogenate samples of the cardiac tissue, a decrease was observed in the 2nd group ($p < 0.01$) compared to the control group. While a change was not observed in the CAT enzyme activity of liver tissues, kidney CAT values were established to decrease in the 4th group compared to the 2nd group ($p < 0.05$) (Table 4).

When comparing the MDA concentrations of the hemolysate samples, an increase in the concentration was determined in the 4th group compared to the 2nd group ($p < 0.05$). When analyzing the homogenate samples of heart tissue, a decrease in the MDA amount was established in the 4th group compared to the control group ($p < 0.001$). When comparing the MDA concentrations of the homogenate samples of liver tissue, an increase was observed in the 2nd group compared to the control group ($p < 0.05$). MDA amount was observed to increase in homogenate samples of kidney tissue in the 4th group compared to the 2nd group ($p < 0.05$) (Table 5).

Urine volume was established to increase in the 3rd ($p < 0.001$) and 4th group ($p < 0.001$) compared to the controls. It was also established that urea nitrogen values increased in the 3rd group compared to the control group ($p < 0.001$) and that these values in the 4th group drew near to the control group. It was observed that the uric acid values increased in the 3rd group ($p < 0.001$) and in the 4th group ($p < 0.001$) compared to the control group, and that such an increase in the 4th group was lower. Urine creatine values were observed to rise in the 3rd group compared to the control group ($p < 0.001$). Although an increase was found in the 4th group ($p < 0.001$), it was established to be lower than the 3rd group (Table 6).

Discussion

It was demonstrated in various studies that reactive oxygen species (ROS) that are endogenously synthesized in the human body and that can easily undertake electron exchange with other molecules play an important role in the pathogenesis of hypertension (Ruiz-

Table 5 MDA concentrations of hemolysate, heart, liver and kidney samples in the experimental groups and their statistical analysis

Groups	MDA concentrations			
	Hemolysate (nmol/gHb)	Heart (nmol/ml)	Liver (nmol/ml)	Kidney (nmol/ml)
1. Control	13.95 ± 2.02	26.70 ± 6.51	5.67 ± 0.62	20.48 ± 6.50
2. Tannic acid	14.08 ± 0.79	23.85 ± 7.97	7.04 ± 0.67^{d,b}	11.12 ± 2.47^{f,b}
3. Hypertension	12.99 ± 2.52	20.60 ± 4.56	5.61 ± 0.17	27.27 ± 6.56
4. Hypertension + tannic acid	16.52 ± 2.85^{d}	7.63 ± 1.56^{e,a,c}	6.52 ± 1.42	27.68 ± 5.72^{c}

Compared with the control group ^{a} $p < 0.001$, ^{b} $p < 0.05$. Compared with the tannic acid group ^{c} $p < 0.001$. Compared with the hypertension group ^{d} $p < 0.05$, ^{e} $p < 0.01$, ^{f} $p < 0.001$. The data were summed up as means + SD

Table 6 The values of urinary parameters of the experimental groups and their statistical analysis

Groups	Volume (ml)	pH	Urea nitrogen (mg/dl)	Uric acid (mg/dl)	Urine creatine (mg/dl)
1. Control	4.98 ± 0.21^{a,b,c}	7.91 ± 0.29^{b}	1,568.93 ± 18.44^{b}	8.48 ± 0.30^{e,b,c}	43.56 ± 1.30^{b,c}
2. Tannic acid	4.52 ± 0.30^{d,b,c}	7.67 ± 0.16^{c,f}	1,563.43 ± 12.02^{b}	8.07 ± 0.24^{j,b,c}	42.82 ± 0.65^{b,c}
3. Hypertension	6.77 ± 0.23*^{,a,c}	7.28 ± 0.19*^{,e,c}	1,614.81 ± 16.81*^{,a,i}	9.42 ± 0.39*^{,a}	57.99 ± 6.27*^{,a}
4. Hypertension + tannic acid	5.89 ± 0.24*^{,a,b}	8.13 ± 0.26^{g,b}	1,582.23 ± 8.80^{h}	9.13 ± 0.09*^{,a}	54.13 ± 3.72*^{,a}

Compared with the control group * $p < 0.001$, ^{d} $p < 0.01$, ^{j} $p < 0.05$. Compared with the tannic acid group ^{a} $p < 0.001$, ^{e} $p < 0.05$, ^{g} $p < 0.01$. Compared with the hypertension group ^{b} $p < 0.001$, ^{f} $p < 0.05$, ^{h} $p < 0.01$. Compared with the hypertension + tannic acid group ^{c} $p < 0.001$, ^{i} $p < 0.01$. The data were summed up as means + SD

Gutierrez et al. 2001). Consuming food that has free radical scavenging antioxidant characteristics is an important strategy to prevent hypertension. Therefore, we aimed to investigate the effect of tannic acid which is an hydrolyzed tannin shown to have free radical scavenging properties on essential hypertension.

Systolic blood pressure measurements on the 15th day in 3rd and 4th group administered L-NNA to create hypertension was established to increase. Oktar et al. (2008) administered 0.45 g/l L-NNA in drinking water to rats for 10 days and found a rise in blood pressure values similar to our study. Likewise, the rise seen in our study demonstrates that essential hypertension model occurred in the 3rd and 4th group. The fact that a significant difference was not found in blood pressure values between the control group and the 2nd group shows that tannic acid does not have an effect on blood pressure values in normotensive rats. A decrease was observed in 20th and 30th day blood pressure values of the hypertension group which was statistical different with respect to other initial measurements. This difference may stem from the dose-dependent effect of L-NNA administration. Blood pressure values were found to be low in the 4th group compared to the hypertension group showing the blood pressure reducing effect of tannic acid in hypertensive rats.

The effect of tannic acid on hypertension was indirectly investigated by using nutrients containing tannic acid. Porteri et al. (2010) found that red wine showed a dose-dependent vasodilator effect on patients with essential hypertension and they suggested that such an effect was created by polyphenols or tannic acid contained in red wine. The effect of proanthocyanidin that is among condensed tannins on vein endothelium was investigated in hypertensive rats, and its antihypertensive and vasodilator effect was established (Kawakami et al. 2011). Similar to these studies, the effects of nutrients containing polyphenols or tannin on hypertension were analyzed but the effect of tannic acid that is among the directly hydrolyzed tannins as an active ingredient was not investigated. In order to develop new understandings and treatment methods, it is important to put forth whether natural compounds such as tannic acid have a specific effect.

Kidneys play an important role in keeping the blood pressure within a healthy interval, and thus, blood pressure exceeding a normal level initially affects

kidneys. It was suggested that removing waste materials and excess fluid from the body would be difficult due to damaging blood vessels and filtration in kidneys, and thus, the excess fluid remaining in the blood vessels would raise blood pressure (Zatz and Baylis 1998). Therefore, in our study, by measuring certain urine parameters we aimed to find out how hypertension and tannic acid would affect renal functions in dependence of the doses we used. Baylis et al. (1992) found that chronic nitric oxide synthase inhibition method that we also used in our study created renal damage. Similar to that study, we also established a statistical increase in urea nitrogen, uric acid and urine creatinine values depending on renal dysfunction in the hypertension group. In their study that investigated the toxicity of tannic acid, Robinson et al. established that tannic acid suppress urine production when injected intraperitoneally to rats (Robinson and Graessle 1943). In agreement with Robinson and Graessle, we found that urine volume decreased in tannic acid group compared to the control group. In addition, we also observed that tannic acid we administered after hypertension was created caused a decrease in urine volume compared to hypertension group. When checked through urine volume, it may be suggested that tannic acid has a reducing effect of hypertension. We did not come across with a literature reference demonstrating the effect of tannic acid on urea nitrogen and uric acid values. To sum up, we statistically established that tannic acid has an improving effect on renal functions in the hypertension model.

Oxidative stress is a multisystem case that includes heart, kidney, nervous system, veins, and immune system in hypertension. If reactive oxygen species or free radicals that occur as a result of oxidative stress are not inhibited, they may easily enter electron exchange thanks to the potential they possess. Thus, the balance between free radicals and antioxidant disrupts, and a pathologic environment is occured (Touyz and Briones 2011). In order to reduce the increasing oxidative stress potential in hypertension, it was observed in recent years that the protective characteristics and effect mechanisms of exogenous antioxidants has been in focus. Phenolic compounds attract the attention of researchers the most. It was shown that veratric acid which is a phenolic compound just like tannic acid reduced blood pressure and lipid peroxidation, increased enzymatic and non-enzymatic antioxidant levels in L-NAME-induced hypertensive rats (Saravanakumar and Raja 2011). Increase in blood pressure in hypertension stems from complex interactions in such numerous systems as heart, kidney, brain, liver, and veins (Touyz and Briones 2011). Thus, we investigated the balance condition of free radical–antioxidant in such organs as heart, kidney, and liver in hypertension and whether tannic acid has an effect on it.

We established antioxidant status by analyzing SOD and CAT levels in various organs, and free radical release level by determining MDA concentration. It was observed that tannic acid did not cause a change in the SOD enzyme level in heart and blood following hypertension. The fact that tannic acid administered following hypertension reduced SOD levels in liver leads to believe that tannic acid does not have a positive effect on liver in hypertension. However, an increase was observed in the inhibition values of SOD enzyme of hemolysate and kidney, but this was not statistically significant. When analyzing catalase enzyme levels, it was observed that tannic acid had a reducing effect on antioxidants in hemolysate and kidney samples. There was not an effect of tannic acid on heart and liver samples. In the hypertension model, it was established that only tannic acid had a reducing effect on MDA concentration in heart samples. In a recent study carried out in vitro, it was demonstrated that tannic acid had a free radical sweeping effect and that it increased antioxidant levels while reducing lipid peroxidation (Gulcin et al. 2010). On the other hand, tannic acid was reported to have a pro-oxidant capacity by creating hydroxyl radical in the presence of copper (Khan et al. 2000). A study reported that there were low SOD activity, high MDA concentration and low level of CAT activity in blood samples of hypertensive individuals compared to normotensive individuals. We also observed that CAT activity levels were low in the blood samples.

Based on these findings, tannic acid was observed to have a reducing effect on blood pressure in hypertensive rats. Absence of a statistical difference may be the result of dose or other physiological interactions. It was observed that tannic acid has a reducing effect on urine volume, urea nitrogen, uric acid, and urine creatinine levels determined to increase in hypertensive rats, however, that the said effect on uric acid and urine creatinine was not found

to be statistically significant. In addition, it was observed that tannic acid may cause a statistically significant increase in hemolysate and SOD levels in kidney in hypertension model, and it may also cause a reduction in MDA levels in heart. When comparing our results and previous studies, it was observed that the antioxidant capacity of tannic acid has not yet been fully understood and that it varied depending on different factors. Therefore, further studies are needed in which tannic acid is administered in vivo at different concentrations and the toxicity of which is measured multi-directionally.

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