THE EFFECT OF TELMISARTAN VERSUS GARLIC ON RENAL CORTEX OF EXPERIMENTALLY INDUCED HYPERTENSION IN RATS: A BIOCHEMICAL, HISTOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY

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Abstract: Different metabolic disorders including hypertension cause renal damage and increase the risk of cardiovascular events. Telmisartan, an angiotensin II receptor blocker. Garlic in different forms has antioxidant properties. This study was designed to determine the possible protective effect of telmisartan and garlic on renal cortex of experimentally induced hypertension in rats. Forty adult male albino rats were divided into two groups: Group I; control group (n=10), Group II (n=30); hypertension group. Group II divided into three equal subgroups. Subgroup Iia (hypertension only group), Subgroup Iib (hypertension with telmisartan group); rats were given telmisartan daily oral dose 10 mg/kg/day for 4 weeks from the start of experiment with the induction of hypertension, and subgroup Iic (hypertension with garlic group); rats were given garlic extract i.p. daily dose 500 mg/kg/day for 4 weeks from the start of experiment with the induction of hypertension. Blood and kidney samples and measuring of systolic blood pressure were performed after 4 weeks from the start of experiment. Paraffin sections of kidneys were prepared for histological; H&E and PAS staining and immunohistochemical study for kappa B (kB). The results revealed that the hypertension only group (subgroup Iia) showed high systolic blood pressure (mmHg), elevated blood urea level and serum creatinine with alterations in morphology of renal glomeruli and tubules and strong NF-kB expression. Hypertension with telmisartan group (subgroup Iib) showed significant decreased (P<0.05) systolic blood pressure, blood urea and serum creatinine, NF-kB expression compared with subgroup Iia and showed near normal in morphology of renal glomeruli and tubules. Hypertension with garlic group (subgroup Iic) showed significant decreased (P<0.05) blood urea, serum creatinine, NF-kB expression, insignificant decreased systolic blood pressure with improvement in morphology of renal glomeruli and tubules compared with subgroup Iia. Telmisartan was more effective in hypertension, preservation of normal kidney function and histology than garlic.

Key words: Hypertension, Renal cortex, Telmisartan, Garlic

INTRODUCTION

Hypertension is one of the most frequently occurring diseases worldwide. Approximately 10% of the population with hypertension reveal the secondary type of hypertension [1]. Hypertension has been accepted as one of the most important modifiable risk factors contributing to an increased risk of coronary artery disease and it can also damage the structure and function of organs when it is not controlled well. Hypertension is a disease in which the systemic arteries are both structurally and functionally abnormal [2]. Renovascular hypertension is the most common cause of secondary
hypertension, with a prevalence of 1-2% among hypertensive patients. Renovascular hypertension occurs when the renal arteries carrying the blood to the kidneys become narrowed by plaque build up and less blood flows to the kidneys. The kidneys mistakenly respond as if blood pressure is low and stimulate the release of hormones that increases the blood pressure [3]. Angiotensin II (A-II) is an important vasoconstrictor that regulates systemic and glomerular hemodynamics. In addition, A-II is also known to promote sodium reabsorption, cell growth and extracellular matrix deposition in kidneys. These effects are generally triggered by signaling via angiotensin II type 1 receptors (AT1R). Therefore, AT1R blockade not only improves systemic hypertension but also could provide direct renoprotective effects [4].

Although hypertension is common and readily detectable, but if left untreated it can often lead to lethal complications. Because of high incidence of hypertension and morbidity, various classes of drugs and regimens have been proposed for the control of hypertension. Despite the large armamentarium of drugs being available for the treatment of hypertension, the last two decades have witnessed the introduction of a number of new antihypertensive drugs [5]. Angiotensin II type I receptor (AT1R) blockers are well-known group of drug that indicate principally for the treatment of hypertension as well as for the protection of kidney function in diabetic patients. Telmisartan is a highly selective angiotensin receptor blocker, and the favorable tolerability profile of telmisartan combined with its longelimination half-life ensure the drug provides pronounced reductions in blood pressure (BP) across the entire 24-hour dosage interval [6]. Telmisartan shows antidiabetic effects by activating peroxisome proliferator-activated receptor-γ (PPAR-γ) [7]. Recent evidence shows that telmisartan provides renal benefit at all stages of the renal continuum in patients with type 2 DM. It improves endothelial function in patients with normoalbuminuria, delays the progression to overt nephropathy in patients with microalbuminuria and reduces proteinuria inpatients with macroalbuminuria [8]. Some investigators have shown that telmisartan also possesses anti-inflammatory and antioxidant properties [9].

In recent years much research is focused on the development of herbal medicines which offer exemplary source for drug discovery [10]. Garlic (Allium sativum) is a worldwide traditional food and dietary supplement. Now a days, many garlic preparations are used in the medical field including fresh garlic extract, garlic oil, aged garlic extract (AGE) and a number of organosulfur compounds [11]. Garlic has diverse biological activities, including anti-carcinogenic, antiatherosclerotic, antithrombotic, antimicrobial, anti-inflammatory and antioxidant effects. The more important clinical application is its role as an antihypertensive and protector of the cardiovascular system (12).

The purpose of this study was to determine the possible protective effect of telmisartan and garlic on renal cortex of experimentally induced hypertensive rats.

**MATERIALS AND METHODS**

**Experimental procedure:** In this study, forty adult male albino rats of average weight 150–200 g were used. The animals obtained from the animal house, Moshtohor faculty of Veterinary Medicine, Benha University, Moshtohor city, Egypt. Strict care and cleaning measures were utilized to keep the animal in a normal healthy state; the animals were kept in animal cages under the prevailing atmospheric conditions. All ethical protocols for animal treatment were followed and were supervised by the animal facilities. All animal experiments received approval from the Institutional Animal Care Committee.

**Drugs:** Telmisartan (Boehringer, Ingelheim, Germany) was given orally by gastric tube at a dose of 10 mg/kg/day [7] for four weeks.

**Plant extraction:** Fresh garlic was prepared from a local grower in banha (Egypt). The garlics were chopped, crushed and for extraction macerated with ethanol (96%) for 48 h. Then, it was centrifuged at 200 g for 5 minutes to remove the derbies. The supernatant was filtered and evaporated at 40°C using a rotary evaporator. The extract was stored at -20°C. The frozen extract was then reconstructed with saline to prepare final concentration when needed [13]. It was given intraperitoneally (i.p.) at a dose of 500 mg/kg/day [14] for four weeks.

**Animal grouping:** The rats were divided into two groups as follows:
**Group I** (n=10): Control group. 5 rats as normal control and other 5 rats as sham-operated.

**Group II** (n=30): Hypertensive group which divided into three equal subgroups.

**Subgroup IIa**: Hypertension only group.

**Subgroup IIb**: Hypertension with telmisartan group. Rats were given telmisartan daily oral dose for 4 weeks from the start of experiment with the induction of hypertension.

**Subgroup IIc**: Hypertension with garlic group. Rats were given garlic extract i.p. daily dose for 4 weeks from the start of experiment with the induction of hypertension.

After 4 weeks from the start of experiment then the rats were sacrificed and blood and kidney samples and measuring of systolic blood pressure were performed.

**Induction of hypertension:** The hypertension was induced in rats by ligation of left renal artery. Rats were anaesthetized by ketamine and xylazine (75 mg/kg and 15 mg/kg, i.p. resp.). A 3 cm retroperitoneal flank incision was done. The left kidney was exposed and the renal artery was carefully separated free of the renal vein. The renal artery was then ligated by 4–0 sterile surgical silk. The incision was closed by carefully suturing of the muscle layer with 4–0 silk using a non-cutting needle and the wound was closed with a running 3-0 silk suture [15]. Sham-operated rats were subjected to identical surgical procedures, except that ligation of renal artery was not performed.

**Measurement of blood pressure:** Three consecutive measurements of systolic blood pressure (SBP), which had a difference of less than 5 mm Hg, were considered valid. The mean of these three measurements were recorded as a valid value of SBP on every occasion. The animals that had systolic blood pressure >160 mm Hg were considered hypertensive [16]. Systolic blood pressure was measured by a tail cuff plethysmographic noninvasive methods (Letica LE 5100, panlab, Barcelona, Spain).

**Biochemical studies:** Blood samples were collected from the aortic cannula inheparinized tubes for analytical assays for levels of blood urea (BU), nitrogen and serum creatinine (BC) using a commercial kit, BioAssay System (Hayward, CA 94545, USA). All the assays were performed according to the manufacturer’s instructions.

**Histological studies:** Following laparotomy, right kidney was dissected and excised from each rat and immersed in 10% formal saline. After fixation the tissues were embedded in paraffin blocks and 5 microns thick tissue sections were cut. The specimens were then stained with hematoxylin and eosin (H&E) and with periodic acid-Schiff (PAS) [17]. The mesangial expansion index was scored in four levels from 0 to 3, with the index scores defined as follows: (18):0, normal glomeruli; 1, matrix expansion occurred in up to 50% of a glomerulus; 2, matrix expansion occurred in 50–75% of a glomerulus; and 3, matrix expansion occurred in 75–100% of a glomerulus. Scores were assigned for at least 30 glomeruli from kidney slices from each animal, and the means were calculated.

**Immunohistochemical study:** For the detection of NF-κB expression, immunohistochemistry was applied. Immunohistochemical studies were performed as using a standard avidin-biotin peroxidase complex system according to the kit used (Neomarkers) followed by dianminobenzidine (DAB) visualization [19]. Slides were deparaffinized, rehydrated, rinsed in tap water, and embedded in 3% H2O2 for 10 min to block endogenous peroxidase. The sections were treated initially with 2% trypsin at 37°C for 10 min in order to increase the sensitivity of the immunoperoxidase staining method. Sections were immersed in an antigen retrieval solution (10 mmol/l sodium citrate buffer, pH 6) and subjected to heat-induced antigen retrieval for 20 min in a microwave. Nonspecific protein binding was blocked by a blocking solution (phosphate buffer solution (PBS) and 10% normal goat serum). The slides were incubated for 30 min with the diluted primary antibody using PBS. Monoclonal anti-mouse kappa light chains, Product No. F-0292 Lot 095H4840, were manufactured by Sigma Chemical Co, Cairo, Egypt. Drops of streptavidin peroxidase were added to the slide, left for 20 min, and then washed with PBS for 5 min. Diaminobenzidine was added to slides as a chromogen, after which the slides were washed with distilled water. Finally, the sections were counterstained with hematoxylin, dehydrated, rendered transparent with xylene, mounted and observed under a light microscope [20]. For the negative control the specific primary antibody was replaced by phosphate-buffered saline.

**Morphometric study:** The mean area percentage for PAS reaction within the glomerular tuft
(glomerular matrix index; the ratio of the mesangial matrix area to the glomerular tuft area) and for NF-
êB expression were quantified in 10 images for each group using Image-Pro Plus program version 6.0
(Media Cybernetics Inc., Bethesda, Maryland, USA). PAS reaction and NF-êB expression in subgroup IIb
and IIc compared with subgroup IIa (hypertension only group).

G. Statistical analysis: Statistical analyses were
carried out using IBM SPSS statistics software for
Windows, Version 20 (IBM Corp., Armonk, NY,
USA). All data were expressed as mean ± SD. The
significance of differences between mean values was
analyzed by using the t-test, with P<0.05 as the level
of statistical significance [21].

RESULTS

Blood pressure and biochemical results: The mean
± Sd of systolic blood pressure (mmHg), blood urea
level (mg/dl) and serum creatinine (mg/dl) of all
groups summarized in (Table 1 and histogram 1). It
showed significant (*) decrease in subgroup IIb
compared with subgroup IIa (P <0.05) while this
decrease was insignificant in subgroup IIc.

Histological results with hematoxylin and eosin:
The control group (group I) showed normal histolog-
ic structure of the renal cortex tissue. The
malpighian corpuscles consisted of glomerular
capillaries surrounded by Bowman’s capsule with a
capsular space in between. The parietal layer of the
capsule had a single layer of simple squamous cells,
whereas the visceral layer was lined by podocytes
with large oval nuclei. The renal corpuscles were
surrounded by the proximal convoluted tubule (PCT)
and the distal convoluted tubule (DCT) (Fig. 1).

In hypertension only group (subgroup IIa) glomeruli
showed slight widening of the capsular space with
vacuolations and dark pyknotic nuclei. In some
tubules lumens were dilated with presence of
acellular debris in lumen and others showed
vacuolations in their lining cells cytoplasm with dark
pyknotic nuclei. Interstitial inflammatory cells and
peritubular hemorrhage were observed (Fig. 2).
The hypertension with telmisartan group (subgroup
IIb) showed most of the renal glomeruli and tubules
were normal, but few tubules were slightly dilated
and revealed cytoplasmic vacuolations in their lining
cells (Fig. 3). The hypertension with garlic group
(subgroup IIc) showed few vacuolations with dark
pyknotic nuclei in glomeruli. Some tubules were
dilated with widening of their lumen and others
showed vacuolations in their lining cells cytoplasm
with dark pyknotic nuclei. Peritubular hemorrhage
was also observed (Fig. 4).

Histological results with PAS staining: The control
group showed positive reaction for PAS within thin
basement membrane of Bowman’s capsule, thin
glomerular basement membrane (GBM), diffuse
inter-capillaries mesangia matrix (thin basement
membrane of renal tubules and their brush borders)

Explanation of figures

Fig. 1. A photomicrograph of a section of the renal cortex of a control group (group I) showing renal corpuscles with glomerular
capillaries (G) surrounded by Bowman’s space (S), proximal convoluted tubule (P) and distal tubule convoluted (D).H&E, ×
400.

Fig. 2. A photomicrograph of a section of the renal cortex of a hypertension group (subgroup IIa) showing slight widening of the
capsular space (S) with vacuolations (V) and dark pyknotic nuclei (arrow). Some tubules were dilated with widening of their
lumen (W) and others showed vacuolations (V) in their lining cells cytoplasm with dark pyknotic nuclei (arrow). Interstitial
inflammatory cells (curved arrow) and peritubular hemorrhage (H) were observed. H&E, × 400.

Fig. 3. A photomicrograph of a section of the renal cortex of a hypertension with telmisartan group (subgroup IIb) showing
dilated few tubules (W) and cytoplasmic vacuolations (V). H&E, × 400.

Fig. 4. A photomicrograph of a section of the renal cortex of a hypertension with garlic group (subgroup IIc) showing vacuolations
(v) and dark pyknotic nuclei (arrow) in glomerulus. Some tubules were dilated with widening of their lumen (W) and others
showed vacuolations (V) in their lining cells cytoplasm with dark pyknotic nuclei (arrow). Peritubular hemorrhage (H) was observed.
H&E, × 400.

Fig. 5. A photomicrograph of a section of the renal cortex of a control group (group I) showing PAS reaction within thin
basement membrane of Bowman’s capsule and GBM (arrow head), diffuse inter-capillaries mesangia matrix (M) and in thin
basement membrane of the renal tubules (zigzag arrow). Strong PAS reaction in the brush border (R) of the renal tubules was
noticed. PAS, × 400.

Fig. 6. A photomicrograph of a section of the renal cortex of a subgroup IIa showing PAS reaction within thickened basement
membranes of Bowman’s capsule and GBM (arrow head), mesangial matrix (M) and thick basement membranes of renal
tubules (zigzag arrow). PAS-stained hyaline casts (H) in the lumen of some renal tubules were noticed. PAS, × 400.
The hypertension group (subgroup IIa) showed strong PAS reaction within thickened basement membranes of Bowman’s capsule, GBM, mesangial matrix and thick basement membranes of renal tubules. There was a loss in the PAS-stained brush border in most of the renal tubules. Some renal tubules showed PAS-stained hyaline casts in their lumen (Fig. 6). The hypertension with telmisartan group (subgroup IIb) was nearly similar to control group (Fig. 7), and the hypertension with garlic group (subgroup IIc) showed positive reaction for PAS within relatively thin basement membrane of Bowman’s capsule and GBM, intercapillaries mesangial matrix and in relatively thin basement membranes of the renal tubules. There was a loss in the PAS-stained brush border in few of the renal tubules (Fig. 8).

Immunohistochemical results: The control group showed negative NF-êB expression (Fig. 9). Subgroup IIa showed strong NF-êB expression (areas of brown cytoplasmic staining) in glomeruli and inside and between the renal tubules (Fig. 10) while this expression was very weak in subgroup IIb (Fig. 11) and mild in subgroup IIc (Fig. 12).

Morphometric results: The mean area % of PAS reaction of mesangial matrix for all groups was represented in Tables 2 and histograms 2. There was a significant decreased (P <0.05) in PAS reaction in subgroup IIb and subgroup IIc compared with subgroup IIa. The mean area % of NF-êB expression for all groups was represented in Tables 3 and histograms 3. There was a significant decrease (P <0.05) in NF-êB expression in subgroup IIb and subgroup IIc compared with subgroup IIa.

DISCUSSION

There is a strong relationship between hypertension and chronic kidney disease (CKD). Hypertension is an important cause of end-stage renal disease (ESRD), contributing to the disease itself or, most commonly, contributing to its progression [22]. Renal artery stenosis (RAS) is a leading cause of renovascular hypertension. In a commonly used animal model for RAS, the Goldblatt’s 2-kidney-1-clip (2K1C), the effects of hypertension can be examined in the collateral kidney [23]. The hypertension group (subgroup IIa) in the present study showed high systolic blood pressure (mmHg), elevated blood urea level and serum creatinine with alterations in morphology of renal glomeruli and tubules and strong NF-kB expression in ligation free kidney. In agreement with these findings, a previous studies showed that the renal artery is constricted on only one side with the other artery (or kidney) left untouched which causes sustained increase in BP due to increased plasma renin activity (PRA), which in turn increases circulating angiotensin-II (A-II), a potent vasoconstrictor [24] and is a powerful stimulus for ROS generation [25]). In this model of hypertension, there was high A-II concentrations in the cortical tissue of the clipped and nonclipped kidneys and the inhibition of nitric oxide (NO) synthesis results in an exaggerated increase in the systemic blood pressure and in a decrease in renal blood flow (RBF) in the nonclipped contralateral kidney [26]. Remarkably, activation of the circulating renin-angiotensin system is transient and leads to recruitment of additional pressor pathways, including oxidative stress, sympatho-adrenergic activation, and
independently of BP, which contributes to the maintenance of high BP (28). One of the complications of high blood pressure is the deterioration in renal function, which may lead to an overt renal insufficiency state (26), mesangial cell hypertrophy, extracellular matrix production and thickening of basement membrane (6). Also some authors reported that renovascular hypertension initiates activation of the renin–angiotensin system and structural remodeling, evidenced by fibrosis and vascular deterioration in the affected kidney. Although the renin-angiotensin system tends to resolve once a stable blood pressure (BP) is reached, it has been suggested that transient elevation of plasma A-II could precipitate macrophage infiltration, thereby initiating an inflammatory response within the kidney (29). A-II can activate several intracellular signaling pathways to mediate renal fibrosis and inflammation, including nuclear factor-kappa B (NF-κB), and mitogen-activated protein kinases (30). NF-κB activation regulates neutrophil, macrophage, lymphocyte, and dendritic cell biology. In addition, NF-κB activation has been documented in vivo and in vitro in intrinsic glomerular cells such as podocytes and mesangial, tubular, and endothelial cells in renal injury or after exposure to inflammatory stimuli (31).

Current therapies for human hypertension include angiotensin II (A-II) type I receptor (AT1R) inhibitors, and angiotensin converting enzyme (ACE) inhibitors (32). It has been established that

Table 1: Showing the mean ± SD of systolic blood pressure (mmHg), blood urea level (mg/dl) and serum creatinine (mg/dl) of all groups. Subgroups IIb, IIc compared with subgroup Ia.

<table>
<thead>
<tr>
<th>Group</th>
<th>Systolic Blood Pressure (mmHg)</th>
<th>Blood Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>121.1±3.11</td>
<td>26.69±3.26</td>
<td>0.88±0.11</td>
</tr>
<tr>
<td>IIa</td>
<td>159±7.72</td>
<td>57.89±11.67</td>
<td>2.04±0.21</td>
</tr>
<tr>
<td>IIb</td>
<td>130±5.87*</td>
<td>28.1±3.3*</td>
<td>0.94±0.38*</td>
</tr>
<tr>
<td>IIc</td>
<td>154.2±3.33</td>
<td>47.76±6.14</td>
<td>1.44±0.38*</td>
</tr>
</tbody>
</table>

Table 2: Showing the mean area %, SD of PAS reaction of mesangial matrix in all groups. Subgroups IIb, IIc compared with subgroup IIa. SD=Standard deviation  S=Significant at P<0.05

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean area %</th>
<th>SD±</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>25.76</td>
<td>0.809</td>
<td>0.000</td>
<td>S</td>
</tr>
<tr>
<td>IIa</td>
<td>36.6</td>
<td>1.580</td>
<td>0.000</td>
<td>S</td>
</tr>
<tr>
<td>IIb</td>
<td>26.22</td>
<td>0.94</td>
<td>0.000</td>
<td>S</td>
</tr>
<tr>
<td>IIc</td>
<td>12.27</td>
<td>0.991</td>
<td>0.000</td>
<td>S</td>
</tr>
</tbody>
</table>

Histogram 1: Showing the mean of systolic blood pressure (mmHg), blood urea level (mg/dl) and serum creatinine (mg/dl) of all groups.

Histogram 2: Showing the mean area % of PAS reaction of mesangial matrix in all groups.

Histogram 3: Showing the mean area % of NF-κB expression in all groups.
the angiotensin-II receptor blockers (ARBs) exhibit renoprotective effect; can prevent or slow the progression of kidney damage, in addition to their antihypertensive action in the patients with hypertension [33,34]. Telmisartan is a highly selective angiotensin II type 1 (AT1) receptor antagonist approved for treatment of hypertension [35]. The previous data coincide with the result of the present study as in hypertension with telmisartan group (subgroup IIb) there was significant decreased (P<0.05) systolic blood pressure, blood urea and serum creatinine, NF-kB expression compared with hypertension only group (subgroup IIa) and showed near normal in morphology of renal glomeruli and tubules. Some researchers explain the antihypertension and renoprotective effect of telmisartan as the oxidative stress, apoptosis, involved in the pathogenesis and development of hypertension and the blockade of A-II significantly reduces the levels of proinflammatory mediators and oxidative stress products in various models of inflammation [36]. Telmisartan is a unique ARB with peroxisome proliferator-activated receptor-α activity and this ARB has been reported to offer a more powerful antioxidant effect than other members of the ARB class [4] and antiinflammatory effects of telmisartan showed by attenuation of vascular nuclear factor kappa B (NFkB) activation and tumor necrosis factor [8]. So, the renal damage, inflammation and signaling pathways were ameliorated by telmisartan [37].

Chronic kidney disease (CKD) is associated with hypertension. Patients with mild to moderate renal insufficiency have increased levels of oxidative stress i.e. unfavourable redox balance in which prooxidants gain the upper hand over anti-oxidants. This results in a net increase in reactive oxygen species (ROS), leading to cellular and tissue damage [38]. Medicinal plants and natural herbal products have potential antioxidant activity. Garlic and its compounds which have been reported to have diverse biological activities such as antioxidant, immune modulation and various other biological actions [39].

The hypertension with garlic group (subgroup IIc) in the present study showed significant decreased (P<0.05) blood urea and serum creatinine, NF-kB expression and insignificantly decreased systolic blood pressure and improvement in morphology of renal glomeruli and tubules as compared to hypertension only group (subgroup IIa). The renoprotective effect of garlic in the present study was in agreement with a previous study [40], which reported that S-allylcysteine, a water-soluble nontoxic garlic compound, has antioxidant properties both in vivo and in vitro and treatment with S-allylcysteine was able to ameliorate the increase in serum urea and creatinine and to decrease the histopathological renal damage. In spite of several studies have demonstrated the role of oxidative stress in the pathogenesis of hypertension and its amelioration with the therapeutic strategies that attenuate oxidative stress in rats with chronic kidney disease [41] and that garlic has antihypertensive effect [39,42], garlic failed to significantly decrease the systolic blood pressure in the present study and this agreed with some researchers [43] who reported that treatment with antioxidant has no effect on arterial pressure. Some authors [44,45] attributed this conflict to the use of different garlic preparations, unknown active components and their bioavailability, inadequate randomization, selection of inappropriate subjects and the short duration of trials.

The present study showed that telmisartan was more effective in protection of rats from hypertension and in preservation of normal kidney function and cytoarchitecture than garlic and this explained by some authors who reported that successful management of oxidative stress in a given condition requires in-depth understanding of its cellular and biochemical mechanisms. Consequently, a mere administration of one or more antioxidant vitamins cannot cure oxidative stress in hypertension, renal disease, or other conditions. Instead, specific interventions directed at the specific underlying factor would be most effective. For instance, since hypertension can cause oxidative stress, therapeutic interventions that can reduce blood pressure represent an ideal antioxidant therapy for the hypertension associated oxidative stress. In addition, since stimulation of AT1 receptors by angiotensin II promotes oxidative stress and hypertension via activation and upregulation of NADPH oxidases, drugs that interrupt rennin-angiotensin system can be considered as specific therapies for management of oxidative stress in certain types of hypertension, especially chronic kidney disease [41].

**CONCLUSION**

Telmisartan was more effective in protection of rats from hypertension and in preservation of normal kidney function and histology than garlic.
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REFERENCE