TAURINE ATTENUATES HYPERTENSION AND RENAL DYSFUNCTION INDUCED BY CYCLOSPORINE A IN RATS

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SUMMARY

1. Cyclosporine A (CsA) is the first-line immunosuppressant used for the management of solid organ transplantation and autoimmune diseases. Nephrotoxicity is the major limitation of CsA use. Recent evidence suggests that reactive oxygen species (ROS) play an important role in mediating CsA-induced hypertension and nephrotoxicity. Taurine, the major intracellular free β-amino acid, is known to be an endogenous anti-oxidant and membrane-stabilizing agent. The present study was designed to investigate the effects of taurine on CsA-induced oxidative stress, hypertension and renal dysfunction.

2. Animals were assigned into four groups of seven rats each as follows: (i) control group, receiving vehicle (olive oil; 1 mL/kg, s.c.); (ii) CsA group, given CsA (25 mg/kg per day, s.c.) for 21 days; (iii) taurine group, supplemented with taurine (1% in the drinking water); and (iv) taurine + CsA group, treated with taurine 3 days before and concurrently during CsA injections for 21 days.

3. Cyclosporine A administration elevated blood pressure, reduced serum nitric oxide (NO) levels and deteriorated renal function, as assessed by increased serum creatinine levels and proteinuria and reduced urine flow rate and creatinine clearance compared with vehicle-treated rats. Cyclosporine A induced oxidative stress, as indicated by increased renal tissue concentrations of thiobarbituric acid-reactive substances and reduced concentrations of renal glutathione, glutathione peroxidase and superoxide dismutase. Conversely, no change was noted in renal catalase activity. Moreover, the kidneys of CsA-treated rats showed interstitial inflammation and renal tubular atrophy.

4. Taurine markedly reduced elevated blood pressure, attenuated renal dysfunction and the reduction in serum NO levels and counteracted the deleterious effects of CsA on oxidative stress markers. Furthermore, taurine ameliorated CsA-induced morphological changes.

5. These data clearly indicate the protective potential of taurine against CsA-induced hypertension and nephrotoxicity and suggest a significant contribution of its anti-oxidant property to this beneficial effect.

Key words: catalase, cyclosporine A, glutathione, glutathione peroxidase, hypertension, nephrotoxicity, nitric oxide, superoxide dismutase, taurine, thiobarbituric acid-reactive substances.

INTRODUCTION

Cyclosporine A (CsA) is a cyclic undecapeptidic immunosuppressive agent that has significantly improved long-term survival after organ transplantation and the treatment of autoimmune diseases.1 However, CsA causes a number of side-effects, including renal, hepatic, cardiac, alimentary and neural toxicity.2–4 Hypertension and nephrotoxicity are the most common side-effects that limit the clinical application of CsA.5

Cyclosporine A-induced hypertension is associated with volume expansion and systemic vasoconstriction.6 In addition to its detrimental effect on graft survival,7 hypertension is likely to contribute to the high cardiovascular morbidity in renal transplant recipients.8 The nephrotoxic effects of CsA are functional and structural. They consist of renal afferent vasoconstriction with a concomitant drop in renal blood flow and glomerular filtration rate (GFR)8 and, eventually, the development of afferent arteriolopathy, glomerulosclerosis, tubular atrophy and interstitial fibrosis.8

Several mechanisms have been proposed for CsA-induced nephrotoxicity, such as sodium retention,9 renal vasoconstriction,10 stimulation of the renin–angiotensin system,12 activation of the sympathetic nervous system,13 impaired synthesis of nitric oxide (NO),14 increased synthesis of endothelins,15 induction of transforming growth factor–β16 and alterations in renal prostanooid and thromboxane production.17 Some studies have revealed that a defect in intracellular calcium handling,18 decreased renal dopamine production19 and induction of cytochrome P450 isoenzymes in renal microsomes20 may be involved in CsA nephrotoxicity. However, the exact mechanisms of CsA-induced hypertension and nephrotoxicity remain unknown and have not been fully elucidated.

Reactive oxygen species (ROS) have been suggested to be involved in the pathogenesis of CsA toxicity.21,22 Taurine (2-aminoethanesulphonic acid) is the major intracellular free β-amino acid and is normally present in most mammalian tissues.23 Taurine possesses a number of cytoprotective properties through its actions as an anti-oxidant, osmoregulator and intracellular calcium flux regulator.24 Taurine has been shown to protect against free radical-mediated damage in biological systems, including heart, liver and kidney.22,25–27 Furthermore, taurine has been demonstrated to provide protection in some hypertensive models.28–31 However, the possible actions of...
taurine on hypertension and nephrotoxicity elicited by CsA have not been examined before. The principal aim of the present study was to examine the potential effects of taurine on CsA-induced hypertension and nephrotoxicity in rats.

METHODS

Animals

Normal adult male rats of the Wistar strain, weighing 220 ± 20 g, were used in the present study. All animals were fed standard rat chow and water ad libitum and kept in a temperature-controlled environment (20–22°C) with an alternating 12 h light–dark cycle. The experimental protocol was conducted in accordance with the Institutional Animal Care and Use guidelines of King Saud University and the National Institutes of Health guidelines for the care and use of laboratory animals.

Experimental protocol

Experiments were performed on four groups consisting of seven rats each. The control group was treated with the vehicle, olive oil (1 mL/kg, s.c.) for 21 days. The second group received CsA at a dose of 25 mg/kg per day, s.c., for 21 days.32 Rats in the third group were supplemented with taurine 3 days before and concurrently during CsA injections for 21 days.26,27 The fourth group received taurine on hypertension and nephrotoxicity elicited by CsA have not been examined before. The principal aim of the present study was to examine the potential effects of taurine on CsA-induced hypertension and nephrotoxicity in rats.

Assessment of serum NO

Serum NO levels were estimated indirectly as the main metabolites of NO, namely nitrite and nitrate, by the acidic Griess reaction after reduction of nitrate to nitrite by vanadium trichloride, according to the method described by Miranda et al.35 The Griess reaction relies on a simple colourimetric reaction between nitrite, sulphanomide and N-(1-naphthyl) ethylenediamine to produce a pink azo-product with maximum absorbance at 543 nm. Concentrations were determined using a standard curve of sodium nitrate and results are expressed as µmol/L.

Determination of renal enzyme activities

Determination of TBARS concentrations

The amount of renal TBARS was measured by the thiobarbituric acid assay (TBA), as described previously by Buege and Aust.34 Briefly, 0.5 mL homogenate was added to 2 mL TBA reagent containing 0.375% TBA, 15% trichloroacetic acid and 0.25 mol/L HCl. Samples were boiled for 15 min, cooled and centrifuged at 1 700 g for 15 min at 4°C. The absorbance of the supernatants was measured spectrophotometrically at 532 nm. Thiobarbituric acid-reactive substances concentrations were calculated by the use of 1,1,3,3-tetraethoxypropane as a standard. Results are expressed as nmol/g wet tissue weight.

Measurement of catabolism activity

Catalase activity was measured according to the method described by Higgins et al.30 The decomposition of H2O2 (Aldrich, St Louis, MO, USA) was followed spectrophotometrically at 240 nm in 50 mmol/L potassium phosphate buffer (pH 7.0) with 19 mmol/L H2O2. A 20 µL aliquot of the supernatants was used for 1 mL reaction mixture. The specific activity of catalase was expressed as µmol H2O2 decomposed/min per g renal tissue weight.

Determination of GPX activity

Renal GPX was estimated according to the method described by Paglia and Valentine36 using the Bioxytech GPx-340 kit (Oxis, Portland, OR, USA). Glutathione peroxidase activity was defined as the number of µmol NADPH oxidized/min per g wet tissue weight.

Determination of GSH content

Renal GSH was determined as described previously by Ellman37 and modified by Nagi et al.38 by its reaction with Ellman’s reagent (5,5-dithio-2-nitrobenzoic acid) in phosphate buffer (pH 8.0); absorbance was measured at 412 nm. The GSH concentration was calculated using a standard solution of GSH. Results are expressed as µmol/g wet tissue weight.

Measurement of SOD activity

Renal SOD was measured according to the method described by Sun et al.39 using the Ransod kit (Randox laboratories, Antrim, UK). The principle of the method is based on the inhibition of nitroblue tetrazolium (NBT) reduction by the xanthine–xanthine oxidase system as a superoxide generator. One unit of SOD was defined as the amount of enzyme causing 50% inhibition in rate of reduction of NBT. Superoxide dismutase activity is expressed as U/mg wet tissue weight.

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Measurement of catalase activity

Catalase activity was measured according to the method described by Higgins et al.30 The decomposition of H2O2 (Aldrich, St Louis, MO, USA) was followed spectrophotometrically at 240 nm in 50 mmol/L potassium phosphate buffer (pH 7.05) with 19 mmol/L H2O2. A 20 µL aliquot of the supernatants was used for 1 mL reaction mixture. The specific activity of catalase was expressed as µmol H2O2 decomposed/min per g renal tissue weight.

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Histopathology

After fixation in 10% buffered neutral formalin, kidneys were dehydrated in an ascending series of alcohol and embedded in paraffin. Serial sections were cut at 3 µm and stained with haematoxylin and eosin. Sections were examined under a light microscope and photomicrographs were taken.
Effect of taurine on CsA nephrotoxicity

Drugs and chemicals
Cyclosporine A (Sandimmun infusion concentrate 50 mg/mL) was obtained from Novartis (East Hanover, NJ, USA) and dissolved in olive oil to a final concentration of 25 mg/mL. Taurine and all other chemicals were purchased from Sigma Chemical (St Louis, MO, USA).

Statistical analysis
Values are expressed as the mean±SEM. Data were analysed by one-way analysis of variance (ANOVA). Tukey’s test was used for pairwise comparisons between treatment groups. Regression analysis was performed to determine parameter correlations. Data were analysed with Systat statistical software (SYSTAT, Chicago, IL, USA). P < 0.05 was considered significant.

RESULTS

Effect of taurine on bodyweight, kidney/bodyweight ratio and renal functions
Cyclosporine A treatment produced a significant (P < 0.01) decrease in bodyweight gain compared with control animals. Treatment with taurine did not affect the weight gain pattern in control or CsA-treated rats (Table 1). No significant changes were observed in the kidney/bodyweight ratio among all treated groups (Table 1). However, CsA-induced nephrotoxicity was reflected by the significant (P < 0.001) increase in serum creatinine level and urinary total protein concentration and the reduction in urine flow rate and Ccr (P < 0.001). Taurine alone had no effect on the kidney function of normal rats. Taurine supplementation improved renal function in CsA-treated rats, as manifested by the significant (P < 0.001) reduction in levels of serum creatinine and urinary protein, whereas urine flow rate and Ccr were greatly increased compared with the group treated with CsA alone (P < 0.001).

Effect of taurine on SBP and HR
As shown in Fig. 1a, SBP was significantly increased after 1, 2 and 3 weeks of treatment from 99 ± 3, 97 ± 4 and 96 ± 4 mmHg, respectively, in normal rats to 125 ± 5, 136 ± 5 and 145 ± 3 mmHg, respectively, in CsA-treated rats (P < 0.01). The CsA-induced elevation in blood pressure was ameliorated by taurine treatment. Systolic blood pressure recordings in the CsA + taurine group were 100 ± 4, 100 ± 5 and 107 ± 5 mmHg after 1, 2 and 3 weeks of treatment, respectively, which was significantly less than the corresponding values in the group treated with CsA alone (P < 0.01). No significant changes were observed in HR among the different groups (Fig. 1b).

Effect of taurine on serum NO level
Cyclosporine A caused a significant reduction in serum NO levels (10.3 ± 0.6 μmol/L) compared with levels in normal control rats.

Table 1  Effect of taurine supplementation (1% in the drinking water) on bodyweight, kidney/bodyweight ratio and renal function in cyclosporine A-treated adult male rats over a period of 21 days

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CsA (25 mg/kg)</th>
<th>Taurine (1% in drinking water)</th>
<th>CsA + taurine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final bodyweight (g)</td>
<td>348 ± 14</td>
<td>270 ± 18*</td>
<td>341 ± 16</td>
<td>278 ± 12</td>
</tr>
<tr>
<td>Kidney weight : bodyweight ratio</td>
<td>0.62 ± 0.033</td>
<td>0.61 ± 0.02</td>
<td>0.67 ± 0.02</td>
<td>0.72 ± 0.03</td>
</tr>
<tr>
<td>Urine flow rate (μL/min per kg)</td>
<td>33.57 ± 2.72</td>
<td>13.6 ± 1.2†</td>
<td>31.87 ± 1.17</td>
<td>27.14 ± 0.74†</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.49 ± 0.04</td>
<td>1.33 ± 0.08†</td>
<td>0.6 ± 0.1</td>
<td>0.91 ± 0.03†</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min per 100 g bodyweight)</td>
<td>0.47 ± 0.04</td>
<td>0.147 ± 0.006†</td>
<td>0.381 ± 0.022</td>
<td>0.33 ± 0.02†</td>
</tr>
<tr>
<td>24 h Urinary protein (g/dL)</td>
<td>365.8 ± 18.9</td>
<td>750 ± 38†</td>
<td>369.7 ± 18.6</td>
<td>563 ± 17†</td>
</tr>
</tbody>
</table>

Values are the mean±SEM (n = 7). *P < 0.01, †P < 0.001 compared with the control group; ‡P < 0.001 compared with the cyclosporine A (CsA)-treated group.

Fig. 1  Effect of taurine supplementation (1% in the drinking water) on (a) systolic blood pressure (SBP) and (b) heart rate (HR) in cyclosporine A (CsA)-treated adult male rats over a period of 21 days. Data are the mean±SEM (n = 7). *P < 0.01, †P < 0.001 compared with the control group (▲); *P < 0.01, **P < 0.001 compared with the CsA-treated group (■). (●), taurine alone; (◆), taurine + CsA.

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Taurine treatment prevented the decrease in NO levels induced by CsA administration (15.57 ± 0.68 μmol/L; $P < 0.001$ compared with the CsA-treated group).

Effect of taurine on renal TBARS

Renal TBARS concentration was increased in CsA-treated rats compared with normal control rats (166.85 ± 4.32 vs 59.28 ± 3.21 nmol/g wet tissue, respectively; $P < 0.001$; Fig. 3). Treatment with taurine inhibited CsA-induced lipid peroxidation and resulted in a significant decrease in TBARS level (90.71 ± 6.24 nmol/g wet tissue; $P < 0.001$ compared with the CsA-treated group).

Effect of taurine on renal catalase activity

As shown in Fig. 4a, there was an increase in renal catalase activity in the CsA group that was not significantly different to that in the control group (214 ± 17 vs 195.8 ± 14.5 μmol/min per g wet tissue, respectively).

Effect of taurine on renal GPX activity

Renal GPX activity was reduced in CsA-treated rats compared with that in normal control rats (3.61 ± 0.15 vs 4.69 ± 0.07 μmol/min per g wet tissue, respectively; $P < 0.001$; Fig. 4b). Taurine alone caused no change in GPX activity (4.62 ± 0.12 μmol/min per g wet tissue) compared with that of the control group. Treatment with taurine ameliorated CsA-induced decreases in GPX activity (4.27 ± 0.01 μmol/min per g wet tissue; $P < 0.01$ compared with the CsA-treated group).

Effect of taurine on renal GSH concentration

Cyclosporine A produced a reduction in renal GSH content compared with that in the normal control group (0.54 ± 0.09 vs 2.03 ± 0.07 μmol/g wet tissue, respectively; $P < 0.001$; Fig. 5a).
Treatment with taurine abrogated the CsA-induced depletion of GSH and increased the GSH concentration up to (1.23 ± 0.12 μmol/g wet tissue, \(P < 0.001\) compared with the CsA-treated group).

**Effect of taurine on renal SOD activity**

Administration of CsA alone caused a significant inhibition in renal SOD activity compared with that in normal control rats (36.43 ± 1.62 vs 54.8 ± 1.9 U/mg wet tissue, respectively; \(P < 0.001\); Fig. 5b). Taurine alone caused no change in SOD activity (57.4 ± 2.6 U/mg wet tissue) compared with that of the control group. Treatment with taurine blunted the CsA-induced decrease in SOD activity (48.1 ± 1.1 U/mg wet tissue; \(P < 0.001\) compared with the CsA-treated group).

**Correlation analysis**

Using combined results from all animals, a significant direct correlation was found between SBP and renal TBARS and the biochemical parameters of renal dysfunction, indicating the role of lipid peroxidation in CsA-induced hypertension and renal injury. Conversely, SBP and renal dysfunction parameters were inversely related to anti-oxidant enzymes, suggesting the importance of internal anti-oxidants in the protection against CsA-induced oxidative damage (Table 2).

### TABLE 2  Correlation coefficients between systolic blood pressure, oxidative stress markers and nephrotoxicity biochemical parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GSH</th>
<th>GPX</th>
<th>MDA</th>
<th>SOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>(r = -0.724^*)</td>
<td>(r = -0.799^*)</td>
<td>(r = 0.881^*)</td>
<td>(r = -0.728^*)</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>(r = -0.845^*)</td>
<td>(r = -0.876^*)</td>
<td>(r = 0.892^*)</td>
<td>(r = -0.744^*)</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>(r = 0.812^*)</td>
<td>(r = 0.743^*)</td>
<td>(r = -0.839^*)</td>
<td>(r = 0.789^*)</td>
</tr>
<tr>
<td>Total urinary protein</td>
<td>(r = -0.823^*)</td>
<td>(r = -0.743^*)</td>
<td>(r = 0.890^*)</td>
<td>(r = -0.787^*)</td>
</tr>
</tbody>
</table>

\(^*P < 0.0001, n = 28.\)

SBP, systolic blood pressure; GSH, reduced glutathione; GPX, glutathione peroxidase; MDA, malondialdehyde; SOD, superoxide dismutase.

**Histopathological studies**

As shown in Fig. 6a,c, the kidneys of the control and taurine-treated rats showed no histopathological changes. However, CsA treatment induced renal tubular atrophy, inflammatory cell infiltration and interstitial fibrosis (Fig. 6b). The distribution was patchy, involving single or multiple tubules in any given area. These structural changes were almost completely abolished with taurine supplementation (Fig. 6d).

### DISCUSSION

Cyclosporine has greatly improved morbidity and mortality in transplantation patients over the past decade and has been increasingly applied with considerable clinical benefit in the treatment of autoimmune diseases. However, its use is often accompanied by unwanted side-effects, such as hypertension and the deterioration of renal function. Previous studies have proposed that ROS production and oxidative stress may contribute to CsA toxicity in many tissues. The present study investigated the effect of taurine on CsA-induced hypertension and nephrotoxicity.

In the present study, CsA induced an increase in blood pressure and renal dysfunction, which was characterized by an increase in serum creatinine and total urinary protein and a reduction in urine flow rate and creatinine clearance. Cyclosporine A nephrotoxicity was confirmed by histopathological changes as atrophied renal tubules and interstitial fibrosis. The administration of CsA has been shown, in other studies, to induce hypertension. It has been suggested that CsA-dependent hypertension may be due to vasoconstriction of the renal microcirculation, resulting in increased renal vascular resistance with a concomitant decrease in GFR. These effects may also account for the increased serum creatinine and reduced creatinine clearance observed in the present study. In addition, CsA-induced renal dysfunction obtained in the present study is consistent with that observed in experimental animals, organ transplant recipients, and healthy controls.

In the present study, CsA increased renal lipid peroxides, measured as TBARS, indicating increased ROS activity and oxidative stress. Cyclosporine A treatment has been shown to increase the
production of free radicals and the formation of lipid peroxides in vivo and in vitro. Cyclosporine A increased malondialdehyde, a stable product of lipid hydroperoxide, in isolated hepatic and renal microsomes. An increase in superoxide radical and hydrogen peroxide following CsA has been demonstrated. Moreover, Zhong et al. have shown that CsA administration results in excess local production of hydroxyl radical, leading to lipid peroxidation and nephrotoxicity. The production of ROS by CsA may be due to the action of CsA as an uncoupler and inhibitor of the mitochondrial electron transport system and CsA metabolism by cytochrome P450 3A. In addition, CsA causes increased renal vascular resistance and decreased renal blood flow. Renal ischaemia, following impaired tissue perfusion, results in the rapid breakdown of tissue ATP with accumulation of the degradation products, inosine, adenosine and hypoxanthine. The enzymatic conversion of hypoxanthine to xanthine by xanthine oxidase generates superoxide radical.

It is well known that an efficient endogenous anti-oxidant defence system operates to combat the production of free radicals. The anti-oxidant enzymes catalase, SOD, GPX and catalase constitute the major defence against ROS-induced oxidative damage. Superoxide dismutase is considered as the first line of defence against the deleterious effects of oxygen radicals in cells, where it scavenges ROS by catalysing the dismutation of superoxide to H$_2$O$_2$ and O$_2$. The decline in renal SOD activity after CsA administration is in agreement with results reported in other studies. Treatment with the SOD mimetic tempol was able to prevent CsA-induced hypertension and renal dysfunction.

Reduced glutathione is sulphur-containing nucleophilic substance found in high concentrations in the kidney. It plays a pivotal role in the protection of cells against oxidative stress and the detoxification of xenobiotics, including CsA. By participating in the glutathione redox cycle, GSH, together with GPX, converts lipid peroxides to non-toxic products, thus maintaining the integrity of the mitochondria and cell membranes. The depletion of GSH stores and a reduction in GPX activity in the kidney obtained in the present study are consistent with other previous investigations. Depletion of renal GSH stores by CsA in the present study could account for the inhibition of renal GPX activity. Vaziri et al. have induced hypertension in normal rats by glutathione depletion. Another study by Inselmann et al. reported enhancement of CsA-induced nephrotoxicity by glutathione depletion. Data obtained from the present study support the link between oxidative stress, hypertension and nephrotoxicity. A similar correlation has been shown by other studies.
Reactive oxygen species can contribute to CsA-induced hypertension and nephrotoxicity by different mechanisms, including inactivation of NO, a direct vasopressor effect and the formation of vasoconstrictive arachidonic acid peroxidation products that can reduce renal blood flow, thus accounting for reduced creatinine clearance.\textsuperscript{50,52}

Nitric oxide is involved in diverse physiological and pathological processes.\textsuperscript{29} In the present study, a decline in serum NO levels was observed in rats treated with CsA. These results are in agreement with those of other studies in experimental animals\textsuperscript{44} and humans.\textsuperscript{53} This decline in serum NO may account for the occurrence of hypertension and renal vasoconstriction, reflected as reduced GFR obtained in the present study. Nitric oxide may react with superoxide radical and form peroxynitrite, which is capable of nitrating the tyrosine residues of proteins and enzymes,\textsuperscript{35} leading to tissue injury. Supplementation with L-arginine, the NO precursor, prevents CsA-induced endothelial dysfunction and hypertension.\textsuperscript{54,55}

Targeting and modulating the internal anti-oxidant mechanisms by chemopreventive agents has become a part of many therapeutic strategies. In the present study, taurine supplementation significantly mitigated CsA-induced oxidative stress markers, reversed the decrease in serum NO levels and abrogated the elevated blood pressure and renal dysfunction. Consistent with our findings, taurine has been demonstrated to lower blood pressure in other different models, including salt-induced hypertensive Dahl rats,\textsuperscript{29} deoxycorticosterone acetate salt rats,\textsuperscript{36} spontaneously hypertensive rats\textsuperscript{41} and fructose-fed hypertensive rats.\textsuperscript{36} Moreover, taurine has been shown to prevent oxidative injury caused by various free radical-generating insults, including ischaemia/reperfusion,\textsuperscript{26} streptozotocin\textsuperscript{26} and cisplatin.\textsuperscript{27} It is not possible to differentiate the extent to which the lowering of blood pressure by taurine contributed to the renal protection obtained in the present study. Nevertheless, the beneficial effects of taurine obtained in the present study are mainly attributed to its anti-oxidant activity.

Taurine can scavenge oxygen free radicals\textsuperscript{23,24} and can act as a membrane stabilizer that can maintain membrane organization against lipid peroxide attack, prevent water influx and, subsequently, avoid cell swelling.\textsuperscript{24} Taurine can stimulate antioxidant machinery contribute to its beneficial actions of taurine. In conclusion, the results of the present study indicate that oxidative damage is responsible, at least in part, for CsA-induced hypertension and kidney dysfunction. The data prove the protective potential of taurine in CsA-induced hypertension and nephrotoxicity. The antilipoperoxidative effect of taurine and its ability to restore the activity of anti-oxidant machinery contribute to its beneficial effects. Further investigations on human subjects would be beneficial, because it may be worth considering supplementation with taurine as part of the renoprotective strategies during CsA therapy.

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