EFFECT OF AMLODIPINE AND LYCOPENE IN AMELIORATION OF RENAL TOXICITY INDUCED BY CISPLATIN IN ALBINO RATS

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ABSTRACT

The present research investigated whether Amlodipine and Lycopene could ameliorate the Cisplatin induced renal toxicity in rats. 80 male albino rats were randomly assigned into 8 equal groups (10 rats each).

**Group 1**: Rats which served as Control group were injected (IP) saline once daily for 20 days. **Group 2**: Rats in this group were served as Saline group and were administrated orally 1 mL saline once daily for 20 days. **Group 3**: Rats in this group were served as Corn Oil group and were administrated orally 1 mL Corn Oil once daily for 20 days. **Group 4**: Rats in this group were served as Amlodipine group and were administrated orally (5 mg/kg/day) Amlodipine once daily for 20 days. **Group 5**: Rats in this group were served as Lycopene group and were administrated orally (10 mg/kg/day) Lycopene once daily for 20 days. **Group 6**: Rats in this group were served as Cisplatin treated group and were injected (IP) (6 mg/kg/day.), once at day 10. **Group 7**: Rats in this group were served as Amlodipine + Cisplatin group and were administrated orally (5 mg/kg/day) Amlodipine once daily for 20 days and injected cisplatin (IP) (6 mg/kg/day) once at day 10. **Group 8**: Rats in this group were served as Lycopene + Cisplatin group and were administrated orally (10 mg/kg /day) Lycopene once daily for 20 days and injected cisplatin (IP) (6 mg/kg /day) once at day 10.

Our results revealed that cisplatin increases urea, creatinine, MDA and potassium level and decreases TAC, GSH, and sodium level while in groups of amlodipine and lycopene showed significant protection to rats' kidney from structural and functional changes associated with...
cisplatin. It can be concluded that Amlodipine and Lycopene could ameliorate the Cisplatin induced renal toxicity.

**KEYWORDS:** Cisplatin, Amlodipine, Lycopene, Renal toxicity.

**INTRODUCTION**
Cisplatin is an antineoplastic drug widely used for the treatment of several human malignancies (as standard component of treatment regimens) including bladder cancer, cervical cancer, Non-small cell lung cancer, ovarian cancer, squamous cell carcinoma of the head and neck, testicular cancer. Nephrotoxicity of cisplatin was the main complication of Cisplatin. Earlier studies reported cardiotoxicity with cisplatin treatment.

Although cisplatin has been a mainstay for cancer therapy, its use is mainly limited by two factors: acquired resistance to cisplatin and severe side effects in normal tissues especially renal tissues. Cisplatin-induced nephrotoxicity is a major complication in the cancer therapy and had a dose limiting toxicity. Nephrotoxicity was reported in the initial clinical trials of cisplatin chemotherapy. Now, it is recognized that the prevalence of cisplatin nephrotoxicity is high, occurring in about one-third of patient undergoing cisplatin treatment.

Amlodipine is a Calcium-channel blocker represents a group of organic chemical structures that share the ability to inhibit Ca^{2+} entry into excitable cells. Calcium channel blockers may help in renal vessel dilatation since there is a key role of voltage-dependent Ca^{2+} channels and intracellular Ca^{2+} stores in the α1A adrenoceptor induced contraction of the renal artery.

There is now great evidence that calcium channel blockers, including amlodipine, have a beneficial nephroprotective effect beyond their blood pressure lowering effect in terms of maintaining glomerular filtration rate, reducing proteinuria, decreasing production of lymphokines and decreasing oxidative stress.

Carotenoids are a group of C-40 isoprenoid-based molecules with > 600 representatives in nature. Lycopene is one of the most representative carotenoids naturally found in plants, bacteria, fungi, and algae. This class of phytochemicals has recently attracted much attention due to potential health beneficial effects associated with carotenoid intake and food rich in carotenoids. Lycopene is mainly available from a very limited list of fruits and vegetables, in contrast to other dietary carotenoids. Red fruits and vegetables, including tomatoes, watermelons, pink-grapefruits, apricots and pink-guavas, are the most common sources of
lycopene. Tomatoes and processed tomato products such as juice, ketchup, paste, sauce and soup all are good sources of lycopene and may account for over 85% of dietary lycopene in the North American diet. The lycopene content of tomatoes varies with the variety and increases with fruit ripening. [17,18]

Therefore; the goal of the present research work was to investigate whether Amlodipine and Lycopene could ameliorate the Cisplatin induced renal and toxicity in rats.

1. MATERIALS AND METHODS

1.1. Tested drugs

Cisplatin (cytoplastin-50®): sterile solution, vial contains 50ml of 50mg (50mg/50ml) cisplatin. It was obtained from cipla company, Egypt. It was administrated at a dose of 6 mg/kg intraperitoneal (IP) once according to.[19]

Amlodipine (Norvasc 5mg®) was obtained from p-fizer, Egypt. It was administrated at a dose of 5 mg/kg orally once daily for 20 days according to.[20]

Lycopene (lycopene 5mg®) was obtained from puritans pride premium, USA. It was administrated at a dose of 10 mg/kg orally in corn oil once daily for 20 days according to.[21]

1.2. Experimental rats

The present study was carried out on a total number of 80 male white Wister albino rats weighting from 150-170 gm. Rats were obtained from Center of Laboratory Animal, Faculty of Veterinary Medicine, Benha University, Egypt. They acclimatized for one week prior to the experiment. All rats received standard laboratory balanced commercial diet and water ad libitum.

1.3. Experimental design

In the present study 80 male albino rats were randomly assigned into 8 equal groups (10 rats each).

Group 1: Rats which served as Control group were injected (IP) saline once daily.

Group 2: Rats in this group were served as Saline group and were administrated orally 1 mL saline once daily for 20 days.

Group 3: Rats in this group were served as Corn Oil group and were administrated orally 1 mL Corn Oil once daily for 20 days.
Group 4: Rats in this group were served as Amlodipine group and were administrated orally (5 mg/kg) Amlodipine once daily for 20 days.

Group 5: Rats in this group were served as Lycopene group and were administrated orally (10 mg/kg) Lycopene once daily for 20 days.

Group 6: Rats in this group were served as Cisplatin treated group and were injected (IP) (6 mg/kg), once at day 10.

Group 7: Rats in this group were served as Amlodipine + Cisplatin group and were administrated orally (5 mg/kg) Amlodipine once daily for 20 days and injected (IP) (6 mg/kg), once at day 10. Group 8: Rats in this group were served as Lycopene + Cisplatin group and were administrated orally (10 mg/kg) Lycopene once daily for 20 days and injected (IP) (6 mg/kg), once at day 10.

1.4. Sampling
Rats were euthanized and blood samples were collected at day 20. Blood samples were collected by puncture of retro orbital plexus from each anesthetized rat with ether. Serum obtained by blood collection in clean dry centrifuge tube. The serum was kept at -20 °C till used in the evaluation of Serum urea, which was determined according to the method described by [22] and serum creatinine was measured according to the method of [23]. Sodium (Na), Potassium (K), were measured according to the methods of [24,25]. Oxidative status was done by determination of malondialdehyde (MDA) level [26] Glutathione (GSH) level [27] and Total antioxidant capacity (TAC) [28] using special diagnostic kits obtained from Laboratory Bio-diagnostic Co.

1.5. Statistical analysis
Statistical analysis was performed using SPSS (Version 20.0; SPSS Inc., Chicago, IL, USA). The significant differences between groups were evaluated by one-way ANOVA using Duncan test as a post hoc. Results are expressed as mean ± SEM. P<0.05 was considered significant.

2. RESULTS
This study was conducted to evaluate the protective efficacy of Amlodipine and Lycopene against nephrotoxic effects of Cisplatin in rats.
3.1. Effect of Amlodipine or Lycopene on Kidney function in normal and Cisplatin treated rats

Serum Urea and Creatinine concentrations showed non-significant increase in Saline, Corn oil, Amlodipine and Lycopene groups when compared to control group. In Cisplatin treated group, serum Urea and Creatinine concentrations showed significant increase when compared to control group, while in Amlodipine + Cisplatin and Lycopene + Cisplatin groups, serum Urea and Creatinine concentrations showed significant decrease when compared to Cisplatin group and these results are shown in table (1).

3.2. Effect of Amlodipine or Lycopene on electrolytes in normal and Cisplatin treated rats

Serum Sodium and Potassium concentrations showed non-significant change in Saline, Corn oil, Amlodipine and Lycopene groups when compared to control group. In Cisplatin treated group, serum Sodium concentration showed significant decrease when compared to control group, while in Amlodipine + Cisplatin and Lycopene + Cisplatin groups, serum Sodium concentration showed significant increase when compared to Cisplatin group.

On the other hand, serum Potassium concentration showed non-significant increase in Cisplatin treated group when compared to control group, while in Amlodipine + Cisplatin and Lycopene + Cisplatin groups, serum Potassium concentration showed non-significant decrease when compared to Cisplatin group and these results are shown in table (2).

3.3. Effect of Amlodipine or Lycopene on Oxidative stress markers in normal and Cisplatin treated rats

Serum MDA concentration, GSH concentration and TAC showed non-significant change in Saline, Corn oil, Amlodipine and Lycopene groups when compared to control group. In Cisplatin treated group, serum MDA concentration showed significant increase when compared to control group, while in Amlodipine + Cisplatin and Lycopene + Cisplatin groups, serum MDA concentration showed significant decrease when compared to Cisplatin. In Cisplatin treated group, serum GSH concentration and TAC showed significant decrease when compared to control group, while in Amlodipine + Cisplatin and Lycopene + Cisplatin groups, serum GSH concentration and TAC showed significant increase when compared to Cisplatin group and these results are shown in table (3).
Table 1: Effect of Amlodipine or Lycopene on Urea and creatinine concentration in normal and Cisplatin treated rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Urea conc.</th>
<th>Creatinine conc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>33.24 ± 0.74</td>
<td>1.00 ± 0.02</td>
</tr>
<tr>
<td>Saline group</td>
<td>32.86 ± 2.97</td>
<td>0.92 ± 0.04</td>
</tr>
<tr>
<td>Corn Oil group</td>
<td>38.74 ± 1.79</td>
<td>0.95 ± 0.03</td>
</tr>
<tr>
<td>Amlodipine group</td>
<td>36.70 ± 1.67</td>
<td>1.01 ± 0.09</td>
</tr>
<tr>
<td>Lycopene group</td>
<td>33.19 ± 1.15</td>
<td>0.92 ± 0.04</td>
</tr>
<tr>
<td>Cisplatin group</td>
<td>74.32 ± 6.71</td>
<td>2.37 ± 0.12</td>
</tr>
<tr>
<td>Amlo+Cis group</td>
<td>35.45 ± 4.81</td>
<td>1.11 ± 0.14</td>
</tr>
<tr>
<td>Lyco+Cis group</td>
<td>36.55 ± 3.34</td>
<td>1.20 ± 0.10</td>
</tr>
</tbody>
</table>

Data are presented as (Mean ± S.E).
S.E = Standard error.
Mean values with different superscript letters in the same column are significantly different at (P<0.05).

Table 2: Effect of Amlodipine or Lycopene on Na concentration (mg/dl) in normal and Cisplatin treated rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Sodium conc.</th>
<th>Potassium conc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>138.75 ± 2.02</td>
<td>5.48 ± 0.15</td>
</tr>
<tr>
<td>Saline group</td>
<td>139.75 ± 1.11</td>
<td>5.63 ± 0.17</td>
</tr>
<tr>
<td>Corn Oil group</td>
<td>139.75 ± 2.02</td>
<td>5.70 ± 0.13</td>
</tr>
<tr>
<td>Amlodipine group</td>
<td>139.75 ± 1.44</td>
<td>5.65 ± 0.24</td>
</tr>
<tr>
<td>Lycopene group</td>
<td>130.00 ± 11.01</td>
<td>5.70 ± 0.17</td>
</tr>
<tr>
<td>Cisplatin group</td>
<td>85.25 ± 3.54</td>
<td>5.60 ± 0.45</td>
</tr>
<tr>
<td>Amlo+Cis group</td>
<td>136.00 ± 4.71</td>
<td>5.75 ± 0.55</td>
</tr>
<tr>
<td>Lyco+Cis group</td>
<td>138.00 ± 1.47</td>
<td>5.80 ± 0.43</td>
</tr>
</tbody>
</table>

Data are presented as (Mean ± S.E).
S.E = Standard error.
Mean values with different superscript letters in the same column are significantly different at (P<0.05).

Table 3: Effect of Amlodipine or Lycopene on MDA concentration (nmol/mL) in normal and Cisplatin treated rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>MDA</th>
<th>GSH</th>
<th>TAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>10.70 ± 0.23</td>
<td>6.33 ± 0.23</td>
<td>2.29 ± 0.08</td>
</tr>
<tr>
<td>Saline group</td>
<td>10.34 ± 0.13</td>
<td>6.05 ± 0.10</td>
<td>2.11 ± 0.10</td>
</tr>
<tr>
<td>Corn Oil group</td>
<td>10.94 ± 0.40</td>
<td>5.99 ± 0.20</td>
<td>2.42 ± 0.22</td>
</tr>
<tr>
<td>Amlodipine group</td>
<td>10.95 ± 0.68</td>
<td>6.00 ± 0.29</td>
<td>2.44 ± 0.23</td>
</tr>
<tr>
<td>Lycopene group</td>
<td>11.56 ± 0.59</td>
<td>6.32 ± 0.17</td>
<td>2.19 ± 0.11</td>
</tr>
<tr>
<td>Cisplatin group</td>
<td>25.27 ± 4.17</td>
<td>3.14 ± 0.29</td>
<td>0.95 ± 0.16</td>
</tr>
</tbody>
</table>
Data are presented as (Mean ± S.E).

S.E = Standard error.

Mean values with different superscript letters in the same column are significantly different at (P<0.05).

4. DISCUSSION

The kidneys are essential organs important for excretion of metabolic waste products as well as preserving chemical homeostasis amongst numerous other functions. The broad use of therapeutic drugs, natural products, environmental pollutants, and industrial chemicals during the last few decades has greatly increased the probability of kidney damage.\cite{29} Determination of the renal excretion of the waste compounds has supplied useful data on the health status of the kidneys.\cite{30} The values of biochemical parameters, such as urea and creatinine, are good indicators of the normal kidney function. For this reason, these parameters have been widely used as indicators.\cite{31}

Cisplatin is one of the potent anticancer agents that is not only cause nephrotoxicity but also induces vascular endothelial dysfunction mediated by inflammation and oxidative stress. Cisplatin-induced nephrotoxicity is a major complication in the cancer therapy and had a dose limiting toxicity.\cite{9} The important parameters that should be taken into account in the evaluation of kidney damage caused by cisplatin are urea and creatinine. These markers are the end products of various metabolic pathways that are excreted in the urine via glomerular filtration whose serum levels are indicator of renal functions. Concerning to biochemical parameters results, rats administrated Cisplatin showed significant increase in serum Urea and creatinine concentrations when compared to control group. These results came in agreement with\cite{32} who reported a significant elevation in the levels of urea and creatinine after Cisplatin administration.

On the other hand, Amlodipine + Cisplatin and Lycopene + Cisplatin groups showed significant decrease in Urea and Creatinine concentrations when compared to Cisplatin group\cite{20} showed that pretreatment with amlodipine (5mg /kg /day) for 4 days before cisplatin administration followed by 3 more days had effectively maintained normal kidney functions. Amlodipine reduced serum urea and serum creatinine and increased serum albumin levels in...
statistically highly significant difference almost to the normal levels. Calcium-channel blockers may help in renal vessel dilatation since there is a key role of voltage-dependent Ca\(^{2+}\) channels and intracellular Ca\(^{2+}\) stores in the \(\alpha1\)A-adrenoceptor induced contraction of the renal artery.

Moreover, the beneficial renal effects of amlodipine, as revealed by effects on serum creatinine in previous studies in hypertensive renal transplant patients.\(^{33}\) The improvements in renal function observed in CsA-treated transplant recipients during amlodipine treatment do not result solely from reductions in BP, as amlodipine significantly reduced serum creatinine, compared to placebo, in normotensive renal transplant recipients treated for 8 weeks.\(^{34}\)

Several antioxidants have been applied to provide protection against chemical induced renal toxicity.\(^{35}\) Lycopene is an efficient free radical scavenger.\(^{36}\) It has been shown to exhibit physical quenching rate constant with ROS.\(^{37}\) Also, it was found to act protector against chemical-induced renal damage in several studies.\(^{38}\)

Treatment diabetic rats with lycopene produced a significantly reduced serum urea level, suggesting its ability to protect against diabetes induced kidney damage, by preventing altered protein metabolism and/or impaired renal function that often exist in diabetes mellitus.\(^{39}\) Moreover, treatment of hyperlipidemic rats with lycopene produced significantly decreased urea and creatinine levels suggesting its nephroprotective effect against hyperlipidemia.\(^{40}\) Also, Administration of lycopene decreased elevated serum creatinine, blood urea nitrogen, renal malondialdehyde induced by gentamicin. They increased reduced glutathione, glutathione peroxidase, superoxide dismutase. It also improved the histopathological changes induced by gentamicin.\(^{41}\)

In the study of\(^{42}\), lycopene administration to cyclosporine-A treated rats resulted in significant amelioration in plasma creatinine and urea levels, kidney tissue TBARs concentrations and GSH-Px and CAT activities. Additionally, lycopene partially recovered cyclosporine-A induced damages include necrotic, degenerative and fibrotic changes in kidney. This status may be explained with partial attenuation of cyclosporine-A induced pathologic changes and decreased lipid peroxidation, and increased antioxidant enzyme activities caused by lycopene administration.
Rats administrated Cisplatin showed significant decrease in serum Na concentration when compared to control group. Moreover, serum K concentration showed non-significant increase in Cisplatin group when compared to control group.

Hyponatremia was the second most common abnormality (88.2%) in the study of.\textsuperscript{[43]} It has been reported to be a common abnormality in many studies.\textsuperscript{[44,45]} In another study, hyponatremia (22.9%) was the only abnormality.\textsuperscript{[46]} Serum sodium increased by 1.35% in the study of,\textsuperscript{[47]} but other electrolytes showed moderately decreased levels. This was attributed to adequate hydration with normal saline during each cycle of chemotherapy. Also, hypokalemia was the least frequent and late appearing electrolyte abnormality.

On the other hand, Amlodipine + Cisplatin and Lycopene + Cisplatin groups showed significant increase in Na concentration when compared to Cisplatin group. These results were in agreement with those of,\textsuperscript{[48]} who reported that there were no particular changes in the plasma levels of sodium and potassium after amlodipine therapy. Previous workers have shown that calcium antagonists have a beneficial effect on the kidney.\textsuperscript{[49]} In fact, amlodipine has been observed to cause a complete reversal of a norepinephrine- induced decrease in the glomerular filtration rate (GFR), and a less significant reversal of the decrease in renal plasma flow. Also, oral administration of lycopene to diabetic rats restored the serum sodium ion level almost close to normal.\textsuperscript{[39]}

In the study of,\textsuperscript{[50]} a statistically significant difference was detected between pre- and post-ischemic Na\textsuperscript{+} values in the control group of rats with induced ischemia. However, Na\textsuperscript{+} value in the lycopene group was not altered despite induction of ischemia. Non-impairment of Na\textsuperscript{+} value after ischemia/reperfusion in the lycopene group has demonstrated protective effect of lycopene on tubular functions.

Regarding to the results of oxidative stress, the rats administrated Cisplatin showed significant elevation in MDA concentration and significant decrease in TAC and GSH concentration when compared to control group.

Oxidative stress injury is actively involved in the pathogenesis of cisplatin induced nephrotoxicity. Reactive Oxygen Species (ROS) directly act on cell components, including lipids. Free radicals damage the lipid components of the cell membrane by peroxidation and denaturation of proteins, which lead to enzymatic inactivation.\textsuperscript{[51]} Lipid peroxidation is
commonly used as marker for the induction of oxidative stress in cells. The level of MDA, which is generated as an end product during the oxidation of lipids, was used as a marker of lipid peroxidation.\textsuperscript{[52]} It has been reported that cisplatin induced nephrotoxicity is closely associated with an increase in lipid peroxidation in the kidney manifested by increased MDA as well as a decrease in anti-oxidant activity with depletion of GSH which is in agreement with the results obtained in the present study.\textsuperscript{[53]}

Glutathione (GSH) is a major non protein thiol in living organisms that plays an important role in protection against free radicals, peroxides, and other toxic the compounds.\textsuperscript{[54]} Platinum sulfhydryl group complexes are taken up by renal cells and stabilized by intracellular GSH for several hours. In case of intracellular GSH depletion, the complexes undergo rapid transformation to reactive metabolites. Thus GSH depletion results in increased toxicity of Cisplatin.\textsuperscript{[55]}

Many studies found that rats treated with cisplatin show significant elevation in plasma, heart, kidney and liver thiobarbituric acid reactive substances (TBARS) while the activities of antioxidant enzymes (SOD and CAT) and the levels of glutathione (GSH) were decreased.\textsuperscript{[56]} Cisplatin significantly increased the intracellular calcium level of renal epithelial cells in a dose-dependent manner. Increased intracellular calcium levels result in oxidative damage and necrosis associated with up regulation of pro-inflammatory cytokines TNF-α, IL-1β, IL-6 and Inducible Nitric-oxide Synthase.\textsuperscript{[57]}

On the other hand, Amlodipine + Cisplatin and Lycopene + Cisplatin groups showed significant decrease in MDA concentration and significant increase in TAC and GSH concentration were observed when compared to Cisplatin group. These results are consistent with Results of,\textsuperscript{[20]} who showed that amlodipine had effectively maintained normal levels of oxidative stress parameters. Amlodipine reduced tissue MDA and increased tissue GSH levels in statistically highly significant difference almost to the normal levels.\textsuperscript{[58]} Reported that, treatment of rats with lycopene protected cells from lipid peroxidation induced by furan and diabetes. Furan exposure and diabetes induced significant decreases in the antioxidant enzyme activities and increases MDA contents and histopathological changes of kidney, but were protected in the presence of lycopene. Moreover, Administration of lycopene decreased elevated renal malondialdehyde induced by gentamicin and increased reduced glutathione, glutathione peroxidase, superoxide dismutase. It also improved the histopathological changes induced by gentamicin.\textsuperscript{[41]}
In the\cite{39} study, the decreased CAT activity in kidney of diabetic animals was significantly improved following oral administration of lycopene. Also, the reports of\cite{59,60} showed that administration of lycopene (90 mg/kg body weight) to streptozotocin-induced hyperglycemic rats caused increased antioxidant enzyme activities (i.e., superoxide dismutase and catalase). In addition, glutathione peroxidase (GPx) is a potent endogenous antioxidant that helps to protect cells from a number of noxious stimuli including oxygen derived free radicals.\cite{61} It is an antioxidant enzyme involved in the detoxification of hydrogen and lipid peroxides and also acts as a peroxynitrite reductase.\cite{62} A significant decrease in GPx activity might be accompanied by a significant increase in lipid peroxidation. Therefore, the increased activity of GPx might be a protective mechanism in response to increased concentrations of H$_2$O$_2$ and other lipid peroxides.

Lycopene’s configuration has been reported to be responsible for its ability to inactivate free radicals and to interfere with free radical- initiated reactions, particularly lipid peroxidation, thereby preventing tissue injury.\cite{63} The antioxidant enzymes are very good biochemical markers of stress and their elevated activity may confirm a potential for remediation.\cite{64} In addition, it has been reported that lycopene has high efficient antioxidant and free radical scavenging capacity.\cite{65} Lycopene has been shown to be one of the best biological suppressants of free radicals, especially those derived from oxygen. It has the highest singlet oxygen quenching rate of all carotenoids in biological systems.\cite{66} The findings of\cite{39} denoted the ability of lycopene to protect the kidney tissue from oxidative damage through elevation of endogenous antioxidant enzymes (SOD, CAT and GPx). The attenuation of kidney tissue in diabetic animals treated with lycopene, which also positively correlated with the significantly reduced kidney MDA level a marker of oxidative stress, further strengthens the notion and also suggests that lycopene may have the ability to protect the kidneys from oxidative injury.

**CONCLUSIONS**

From the present study it was concluded that: Cisplatin is one of the potent anticancer agents that is not only cause nephrotoxicity but also induces cardiotoxicity, after repeated administrations, and anemia. Amlodipine and Lycopene bring all the parameters affected by cisplatin near to normal values. Amlodipine and Lycopene have been shown to be effective against cisplatin induced nephrotoxicity as it showed marked improvement in biochemical, tissue damage and oxidative changes in kidney. Thus Amlodipine and Lycopene have
protective effect which minimizes the nephrotoxicity induced by cisplatin, thereby suggesting their use as potent nephroprotective agents.

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