Comparative evaluation of protective effects of green tea and lycopene in potassium dichromate-induced acute renal failure in rats

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ABSTRACT

The aim of this study was to compare the effects of green tea extract and lycopene on potassium dichromate-induced acute renal failure (ARF) and oxidative stress in rats. ARF was induced by subcutaneously (s.c) injection of a single dose (15 mg/kg) potassium dichromate (PD). Rats were randomly divided into 6 groups treated daily for 14 days with green tea (600 mg/kg) and/or lycopene (4 mg/kg) as follow: Group I: Green tea control group received saline. Group II: Lycopene control group received corn oil. Group III: Rats injected s.c with PD and served as kidney damaged group. Group IV, V and VI: Rats received green tea, lycopene and its combination, respectively, before PD injection. Biochemical analysis were utilised for evaluation of the kidney damage such as: creatinine and urea in serum, total protein in urine, malondialdehyde and reduced glutathione contents as well as catalase and superoxide dismutase activities were determined in kidney tissue and finally histopathological study. Injection of PD to rats induced a marked renal failure, characterized with a significant increase in serum creatinine and urea as well as urine total protein. PD group had higher kidney malondialdehyde, lower reduced glutathione content and catalase activity. Pre-treatments with green tea extract and/or lycopene ameliorate kidney damage which reflect improvement of biochemical indices and histopathological study. Results from this study indicate that green tea extract alone or with lycopene might have protective effect against potassium dichromate-induced ARF and oxidative stress in rat more than lycopene alone.

Keywords: Kidney damage; Oxidative stress; Green tea; Lycopene; Rat

INTRODUCTION

Acute renal failure (ARF) is characterized by a rapid, potentially reversible, decline in renal function including rapid fall in glomerular filtration rate (GFR) and retention of nitrogenous waste products over a period of hours or days. The mortality rate of patients with ARF has remained 25–70% despite the use of various pharmacologic agents[1]. ARF is defined as a percentage increase in serum creatinine to 3 times the baseline value or more in the last 48 hours [2].

Potassium dichromate, PD, (K₂Cr₂O₇) is widely used in metallurgy, chrome plating, chemical and stainless steel industry, textile manufacture, wood preservation, photography, photoengraving and cooling systems [3]. Chromate could be found in drinking water source supplies as a contaminant resulting from various industrial processes. Environmental contamination has led to elevated levels of chromate in drinking water across the U.S. and in many parts of the world [4]. Occupational exposure to chromium (Cr) is common with welders, chrome-plating workers, and chromium pigment factories workers [5, 6]. The oxidation state and solubility of chromium compounds determine their toxicity. In contrast to chromite, which is naturally occurring form and an essential trace element for humans and others mammals, chromate compounds are highly toxic. They induce dermatotoxicity, immunotoxicity, genotoxicity and carcinogenicity [7]. In biological systems, once chromate is absorbed, it is distributed in the liver, lung, spleen, kidney and heart [8] and causes oxidative damage in hepatocytes, brain [9] and kidney [10]. PD-
induced ARF in rat mimics the occupational hazard. Chromium nephrotoxicity is thought to occur through the oxidant lesion mechanism. There is still a lack of specific remedies against chromium nephrotoxicity [11].

Tea (Camellia sinensis) is one of the most commonly consumed beverages since ancient times. It is still the beverage most available to general populations in many countries all over the world[12]. Tea contains several antioxidants, mainly polyphenols namely, catechins in green tea and theaflavin in black tea. Catechins have recently received a lot of attention owing to its role as an antioxidant[13] and their ability to protect the human body from exposure to different diseases [14]. Catechins can scavenge a wide range of free radicals, including the most active OH radical, which initiates lipid peroxidation. Consequently they terminate initiation and propagation of lipid peroxidation [15]. Furthermore catechins can scavenge both O₂⁻ and LOO radicals [16], NO radical [17], ONOO⁻ [18], carbon-center free radicals and 'ÖO₂[19]. It has been reported that, catechins have many protective effects on the cardiovascular system, they exert an antihypertensive [20], anti-atherosclerotic, anti-hypcholesterolemic and antihypertrphy effects [21] and they are used as folk remedies for inflammatory diseases [22]. Recently, green tea extract attenuated alcohol-induced oxidative injury and lipogenesis in the liver by the synergetic action of catechins and caffeine [23] and improves hypertension and insulin resistance in a rat model of metabolic syndrome through reduction of ROS [24].

Lycopene is a major carotenoid, available primarily from tomatoes and its products [25]. Carotenoids are among the most common natural pigments [26] and responsible for many of the red, orange, and yellow hues of plant leaves, fruits, and flowers. Only plants, bacteria, fungi, and algae can synthesize carotenoids, but animals get them from diet [27]. Lycopene, exhibit the highest physical quenching to Ö² has a high antioxidative activity and a protective effect in various diseases [28]. Lycopene has attracted considerable attention as a potential chemopreventive agent [29]. There is substantial evidences demonstrating an inverse relationship between the consumption of lycopene and the risk of a wide variety of cancers [30] including cervical cancer [31], urinary bladder cancer [32], buccal pouch carcinogenesis 33 and gastric carcinogenesis [34]. One of the important effects of lycopene is its ability to protect DNA by reducing its oxidative damage in vitro and in vivo [35-37]. Lycopene also, prevent the side effects of chemotherapy due to its antioxidant and anti-inflammatory properties [38] and now, prevent chronic diseases induced by oxidative stress related to high fat diet [39].

Accordingly, the present study aimed to compare the possible protective effects of the natural antioxidants namely green tea, lycopene and their combination on some changes produced by experimentally induced kidney damage in rats.

**EXPERIMENTAL SECTION**

2.1. Animals
Adult male Sprague-Dawley albino rats weighing 120 – 140g purchased from the animal house colony of the National Research Center (Dokki, Giza, Egypt) and were kept in the animal house under conventional laboratory conditions. Experiments were performed according to the National Regulations of Animal Welfare and Institutional Animal Ethical Committee (IAEC).

2.2. Chemicals
Potassium dichromate was obtained from NRC, Giza, Egypt. Glutathione, 5,5_-dithio-bis-(2-nitrobenzoic acid), thiobarbituric acid (TBA) and 1,1,3,3-tetraethoxypropane were obtained from Sigma Aldrich Chemical Co. (USA). All other chemicals were of the highest available commercial grade.

2.3. Drugs
a) Green tea water extract in the form of powder (Technomate for Chemicals and Pharmaceuticals, Egypt).

b) Lycopene in the form of powder (El-Debeiky Pharma Co., Egypt).

2.4. Experimental design
ARF was induced by administration of a single dose of PD (15 mg/kg, subcutenously) [40]. Animals were divided into 6 groups treated daily for 14 days with green tea (600 mg/kg) [41], lycopene (4 mg/kg) [42] or combination of green tea and lycopene before induction of ARF with PD as follow: Group I: Green tea control group received saline. Group II: Lycopene control group received corn oil. Group III: Rats injected s.c with PD and served as kidney damaged group. Group IV, V and VI: Rats received green tea, lycopene and its combination, respectively. After 2, 14 days following the last treatment, samples were taken as follows: urine was collected and filtered for determination of creatinine. Under light ether anesthesia, blood samples were taken from the abdominal aorta and used for determination of blood urea nitrogen, total protein and creatinine levels. The animals were killed by
cervical dislocation, and the two kidneys from each rat were immediately dissected out, washed with ice-cooled physiological saline and homogenized in 0.15M KCl solution. Aliquots of the homogenate were prepared for determination of tissue contents of reduced glutathione (GSH) and malondialdehyde (MDA) as well as the enzyme activities of catalase (CAT) and superoxide dismutase (SOD).

2.5. Biochemical analysis
The following parameters, indicating glomerular, tubular and oxidative kidney damage, were measured after 2 days and 14 days of induction of kidney damage. Body weight was determined. BUN level was determined following the colorimetric method of Berhelot reaction [43], while creatinine clearance (Ccr) was calculated after estimating the serum and urinary creatinine levels by the alkaline picrate method [44]. Total protein level was determined in urine samples using Biodiagnostic kits [45]. GSH and MDA in kidney tissue were determined [46, 47], respectively. Measurement of enzyme activities of catalase (CAT) and superoxide dismutase (SOD) were carried out in kidney homogenate [48, 49].

2.6. Histopathological studies
One kidney specimens was separated from the animal immediately after sacrifice and opened along convex side to ensure complete fixation. All the specimens were fixed in 10% formal saline for at least 72 h then washed with water and processed to obtain 4-6 Mm section. They were stained with hematoxilin-eosin for histopathological examination.

2.7. Data analysis
Data are expressed as mean ± S.E. Analysis was done using ANOVA followed by the Tukey–Kramer test for multiple comparisons. A 0.05 level of probability was used as the criterion for significance.

RESULTS
No statistical difference in body weight was observed among treated and control groups. Induction of kidney damage by PD significantly decreased Ccr to 28.98% after 2 days and 78.04% after 14 days of induction, as compared with normal control group. The pre-treated animals with green tea extract, lycopene and their combination significantly increased Ccr to 191.66%, 173.33% and 198.33%, respectively, after 2 days of induction and 124.37%, 120.62% and 123.75%, respectively, after 14 days of induction of kidney damage, as compared with the kidney damaged group (Table 1, 2).

Table 1
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (Saline)</th>
<th>Control (Oil)</th>
<th>PD</th>
<th>PD+GT</th>
<th>PD+LY</th>
<th>PD+GT+LY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight</td>
<td>10.16±0.16</td>
<td>10.83±0.83</td>
<td>9.16±0.54</td>
<td>10.33±0.33</td>
<td>9.66±0.33</td>
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<tr>
<td>Ccr</td>
<td>2.07±0.17</td>
<td>2.06±0.15</td>
<td>0.60±0.02 *</td>
<td>1.15±0.1 *</td>
<td>1.04±0.08 *</td>
<td>1.19±0.07 *</td>
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<tr>
<td>Creatinine</td>
<td>0.25±0.01</td>
<td>0.24±0.01</td>
<td>1.12±0.06 *</td>
<td>0.41±0.02 *</td>
<td>0.44±0.03 *</td>
<td>0.39±0.01 *</td>
</tr>
<tr>
<td>BUN</td>
<td>14.94±0.14</td>
<td>15.47±0.88</td>
<td>60.00±0.25 *</td>
<td>31.29±0.71 *</td>
<td>39.26±0.20 *</td>
<td>29.99±0.29 *</td>
</tr>
<tr>
<td>Total protein</td>
<td>20.94±0.12</td>
<td>20.99±0.71</td>
<td>84.03±0.90 *</td>
<td>48.06±0.49 *</td>
<td>60.82±0.59 *</td>
<td>46.35±0.32 *</td>
</tr>
</tbody>
</table>

GT: green tea; LY: lycopene; PD: potassium dichromate
Data were expressed as mean ± SE (n=6).
Statistical analysis was carried out by one-way ANOVA followed by Tukey multiple comparisons test.
* Significantly different from normal control (Saline) at P<0.05.
* Significantly different from corn oil control group at P<0.05.
* Significantly different from kidney damaged group at P<0.05.

Table 2
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (Saline)</th>
<th>Control (Oil)</th>
<th>PD</th>
<th>PD+GT</th>
<th>PD+LY</th>
<th>PD+GT+LY</th>
</tr>
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<tbody>
<tr>
<td>Body weight</td>
<td>28.33±2.10</td>
<td>29.16±2.00</td>
<td>28.33±1.66</td>
<td>28.16±1.53</td>
<td>28.33±1.66</td>
<td>29.33±1.66</td>
</tr>
<tr>
<td>Ccr</td>
<td>2.05±0.06</td>
<td>2.03±0.17</td>
<td>1.00±0.07 *</td>
<td>1.99±0.07 *</td>
<td>1.93±0.18 *</td>
<td>2.02±0.09 *</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.24±0.007</td>
<td>0.25±0.01</td>
<td>0.38±0.007 *</td>
<td>0.26±0.01 *</td>
<td>0.26±0.007 *</td>
<td>0.25±0.01 *</td>
</tr>
<tr>
<td>BUN</td>
<td>14.77±0.31</td>
<td>15.16±0.73</td>
<td>32.69±1.37 *</td>
<td>20.88±1.20 *</td>
<td>23.15±1.88 *</td>
<td>18.47±0.92 *</td>
</tr>
<tr>
<td>Total protein</td>
<td>21.18±0.007</td>
<td>21.22±0.02</td>
<td>36.37±1.17 *</td>
<td>23.79±0.04 *</td>
<td>25.44±0.04 *</td>
<td>21.99±0.07 *</td>
</tr>
</tbody>
</table>

GT: green tea; LY: lycopene; PD: potassium dichromate
Data were expressed as mean ± SE (n=6).
Statistical analysis was carried out by one-way ANOVA followed by Tukey multiple comparisons test.
* Significantly different from normal control (Saline) at P<0.05.
* Significantly different from corn oil control group at P<0.05.
* Significantly different from kidney damaged group at P<0.05.
Fig 1: Effect of pre-treatment with green tea extract (600 mg/kg, orally) and/or lycopene (4 mg/kg, orally) on A. malondialdehyde (MDA) and B. reduced glutathione (GSH) content as well as C. catalase (CAT) and D. superoxide dismutase (SOD) activity of kidney damaged rat

Data were expressed as mean ± SE (n=6).
Statistical analysis was carried out by one-way ANOVA followed by Tukey multiple comparisons test.

a Significantly different from normal control (Saline) at P<0.05.
b Significantly different from corn oil control group at P<0.05.
c Significantly different from kidney damaged group at P<0.05.

Induction of kidney damage by PD produced a significant increase of serum creatinine and BUN to 448% and 401.60% respectively after 2 days and to 158.33% and 221.32% respectively after 14 days of induction, as compared with the normal control group. The pre-treatment of animals with green tea extract, lycopene and their combination significantly reduced serum creatinine to 36.60 %, 39.28% and 33.82%, respectively and BUN to 52.15%, 65.43% and 49.98%, respectively, after 2 days of induction, as compared with the kidney damaged group. Also, after 14 days of induction of kidney damage, serum creatinine was significantly reduced in animals pretreated with green tea extract, lycopene and their combination to 68.42%, 68.42% and 65.78%, respectively, and BUN to 70.81% and 56.50%, respectively, as compared with the kidney damaged group (Table 1, 2).

Kidney tissue malondialdehyde content was significantly increased in kidney damaged group with PD to 248.25% after 2 days and 156.56% after 14 days of induction, as compared with the normal control group. The pre-treatment with green tea extract, lycopene and the combination of both drugs significantly decreased kidney tissue malondialdehyde content to 73.97%, 84.80% and 70.20%, respectively, after 2 days and 77.09%, 85.10% and 75.04%, respectively, after 14 days of induction of kidney damage, as compared with the kidney damaged group (Fig. 1A).
Data in Fig. 1B indicate that induction of kidney damage by PD significantly reduced GSH content in kidney homogenates to 15.38% after 2 days and 65.38% after 14 days of induction, as compared with the normal control group. A significant increase of GSH content in kidney homogenates was observed in the pre-treatment with green tea extract, lycopene and the combination of both drugs to 525%, 475% and 550%, respectively, after 2 days of induction, and 135.29%, 129.41% and 141.17%, respectively, after 14 days of induction of kidney damage, as compared with the kidney damaged group.

Induction of kidney damage by PD produced a significant decrease of CAT activity in kidney to 35.57% after 2 days and 65.78% after 14 days of induction, as compared with the normal control group. CAT activity was significantly elevated in the pre-treatment with green tea extract and its combination to 139.91% and 147.30% after 2 days and 123.38% and 125.21% after 14 days of induction of kidney damage while no significant change of CAT activity was observed in the pre-treatment with lycopene after 2 days or 14 days of induction of kidney damage, as compared with the kidney damaged group (Fig. 1C). No statistical difference in SOD was observed among all treated and control groups at all time point (Fig. 1D).

Histopathology study of kidney tissue section obtained from a normal rat receiving saline or corn oil showing normal proximal convoluted tubule (P), distal convoluted tubule (D) and renal corpuscles composed of a tuft of capillaries forming the glomerulus (G) (Figure 2A & B). Kidney tissue section from a rat damaged with PD showing dilatation of most of the tubules being more observed in the proximal tubules, which loose their brush borders. This dilatation is due to atrophy of the lining epithelium of these tubules. Many tubules suffer from degeneration of their lining epithelium with spots of hemorrhage in the interstitial tissue in between the tubules, after 2 days of administration (Figure 2C). Kidney tissue section of a rat damaged with PD showing normal renal corpuscles, proximal (P) and distal (D) convoluted tubules except for a very few tubules that appeared dilated. In between the functional kidney tissue blood vessels are markedly dilated and congested with blood. Cellular infiltrates are observed near the congested blood vessel, after 14 days of administration (Figure 2D). Kidney tissue section from a damaged rat pre-treated with green tea extract showing dilatation of few tubules. Other tubules show mild vacuolar degeneration of their lining epithelium, after 2 days of kidney damage (Figure 2E). Kidney tissue section from a damaged rat pre-treated with green tea extract showing a quite normal kidney tissue, after 14 days of kidney damage (Figure 2F). Kidney tissue section from a damaged rat pre-treated with lycopene showing dilatation of many renal tubules and obvious vacuolar degeneration of the lining epithelium of both types of these tubules. However, renal corpuscles (G) appear nearly normal, after 2 days of kidney damage (Figure 2G). Kidney tissue section from a damaged rat pre-treated with lycopene showing mild dilatation of some renal tubules most of them are of the distal type. Many of the tubules especially the proximal ones (P) are normal as well as the glomeruli (G) after 14 days of kidney damage (Figure 2H). Kidney tissue section from a damaged rat pre-treated with green tea extract and lycopene showing a area of normal renal tissue containing both proximal (P) and distal (D) convoluted tubules. Another area is seen where few of the tubules show vacuolar degeneration of their epithelium. Neither dilatation nor congestion is observed. Cellular infiltrates are negatively appeared, after 2 days of kidney damage (Figure 2I). Kidney tissue section from a damaged rat pre-treated with green tea extract and lycopene showing most of the renal tubules are normal in shape as well as the renal glomerulus, after 14 days of kidney damage (Figure 2J).
Fig. 2: Photomicrographs of sections of the kidney tissue of: (A) a normal rat receiving saline showing normal proximal convoluted tubule (P), distal convoluted tubule (D) and renal corpuscles (arrow) composed of a tuft of capillaries forming the glomerulus (G). (B) a normal rat receiving corn oil showing the same normal structure of control group (C) a rat damaged with PD showing dilatation of most of the tubules (arrow) being more observed in the proximal tubules, which loose their brush borders. This dilatation is due to atrophy of the lining epithelium of these tubules. Many tubules suffer from degeneration of their lining epithelium with spots of hemorrhage (arrow heads) in the interstitial tissue in between the tubules, after 2 days of administration. (D) a rat damaged with PD showing normal renal corpuscles, proximal (P) and distal (D) convoluted tubules except for a very few tubules that appeared dilated. In between the functional kidney tissue blood vessels are markedly dilated and congested with blood (arrow head). Cellular infiltrates (arrow) are observed near the congested blood vessel, after 14 days of administration. (E) a damaged rat pre-treated with green tea extract showing dilatation of few tubules (arrow head). Other tubules show mild vacuolar degeneration of their lining epithelium (arrow), after 2 days of kidney damage. (F) a damaged rat pre-treated with green tea extract showing a quite normal kidney tissue, after 14 days of kidney damage. (G) a damaged rat pre-treated with lycopene showing dilatation of many renal tubules (arrow head) and obvious vacuolar degeneration (arrow) of the lining epithelium of both types of these tubules. However, renal corpuscles (G) appear nearly normal, after 2 days of kidney damage. (H) a damaged rat pre-treated with lycopene showing mild dilatation of some renal tubules (arrow) most of them are of the distal type. Many of the tubules especially the proximal ones (P) are normal as well as the glomeruli (G) after 14 days of kidney damage. (J) a damaged rat pre-treated with green tea extract and lycopene showing a area of normal renal tissue containing both proximal (P) and distal (D) convoluted tubules. Another area is seen where few of the tubules show vacuolar degeneration of their epithelium (arrow). Neither dilatation nor congestion is observed. Cellular infiltrates are negatively appeared, after 2 days of kidney damage. (J) a damaged rat pre-treated with green tea extract and lycopene showing most of the renal tubules are normal in shape as well as the renal glomerulus, after 14 days of kidney damage. (Hx. & E X 400)
DISCUSSION

Potassium dichromate (PD) was used to induce oxidative kidney damage [50]. The kidney damaging effect of chromium (Cr) is achieved via its accumulation in vacuoles inside the proximal tubular cells. This may lead to slow excretion and remaining of Cr in the kidney for long time [51]. Chromate is easily taken up by cells through the sulfate anion transport system. Once inside the cell, chromate is reduced through reactive intermediates to the more stable form chromite by cellular reductants including glutathione, vitamin C, vitamin B2 and flavoenzymes [52]. This reduction process generates free radical species such as active oxygen radicals, which are involved in the cytotoxic effects of Cr [3].

The present results showed that, the induction of kidney damage by PD did not significantly change body weight of rats after 2 and 14 days of induction, as compared with the normal control group (Table 2, Fig 2). These results are in harmony with previous study [53] and suggest that, PD administration might not on affect water or food consumption in rats [54].

Results of the current study revealed that, the induction of kidney damage by PD produced a significant increase of urine volume to 163.26% after 2 days of induction. This effect might be attributed to the loss of brush border of the proximal tubules which is an early feature associated with alterations in transport of water by breaking gap junctions, leading to increased permeability [55]. The present histopathological results showed significant structural abnormalities of the kidney after PD administration, specifically, after 2 days of induction, where the epithelium of the proximal convoluted tubular cells showed dilatation, necrosis and degeneration. After 14 days of induction of kidney damage, the urine volume of kidney damaged animals was increased to 120.61%, as compared with the normal control group. The present histopathological results cleared that, the proximal tubules showed partial regeneration of their lining epithelium, suggesting the occurrence of multiple cycles of injury and repair. These results are in agreement with previous investigations using PD [56]. In the present study, the pre-treatment of animals with green tea and/or lycopene significantly reduced the urine volume after 2 and 14 days of induction of kidney damage, as compared with the kidney damaged group. The histopathological study proved that, the pre-treatment with green tea and/or lycopene showed a quite normal kidney tissue. This observation is consistent with previous studies using naringin[57]. The present results might reflect the ability of green tea and lycopene to restore the brush border of the renal tubules with its glyocalyx of the epithelial lining allowing them to perform their absorbing function properly.

In the present study, induction of kidney damage using PD produced a significant increase of serum creatinine, blood urea nitrogen (BUN) and total protein and decrease Ccr after 2 and 14 days of induction, as compared with the normal control animals and might be attributed to the decreased glomerular filtration rate and renal blood flow secondary to renal vasoconstriction that eventually results in tubular damage. While, the pre-treatment of animals with green tea and/or lycopene significantly reduced serum creatinine, BUN and total protein in urine and increase Ccr after 2 and 14 days of induction of kidney damage, as compared with the kidney damaged animals. These findings are in agreement with previous studies using naringin and lycopene [42]. Kidney function appears to be improved by green tea catechin due to its antithrombotic action [58], which in turn controls the arachidonic acid cascade system including prostaglandin E2, one of the major prostanooids products generated by prostaglandin synthase in the kidney and commonly causes renal vasodilation and increases glomerular filtration rate [59]. Also the beneficial effects of carotenoids, may be explained by decreasing vasoconstriction via upregulation of expression of angiotensin-converting enzyme and through inhibition of the expression of the expression of renal renin, angiotensinogen and angiotensin type 1 receptor [60]. Moreover carotenoids may prevent proteinuria by protecting the podocytes (renal epithelial cells) from injury leading to decreased ROS and increased glomerular filtration rate [61].

Several studies reported that, chromium reaches the peak value in serum and kidney one day after administration, and then its concentration gradually decreases in serum more than the kidney [62]. Previous pharmacokinetic studies also proved that, chromium is rapidly distributed and its half life is longer in the kidney than blood serum [63]. In the present work, the renal oxidative stress induced by PD was proved clearly by the increase of malondialdehyde (MDA), after 2 and 14 days of induction of kidney damage, as compared with normal control animals. A similar pattern was recorded by another study [54]. These results suggest that, oxidative stress might contribute to cell damage in a variety of kidney diseases. Moreover previous studies reported the production of free radical species essentially hydrogen peroxide (H2O2), nitric oxide (NO) and other reactive species by PD. These free radicals attack lipid components leading to lipid peroxidation [64]. The pre-treatment of animals, in the present study, with green tea and/or lycopene produced a significant reduction of kidney MDA content after 2 and 14 days of induction of kidney damage, as compared with the kidney damaged control. These results are in agreement with previous studies using green tea and lycopene [41, 65]. These results suggest that, green tea and/or lycopene might prevent the
deleterious consequences of biological membrane peroxidation caused by PD via the polyphenolic compounds, catechins [66], which can scavenge free radicals and lycopene also.

It is well known that endogenous antioxidant enzymes are responsible for preventing and neutralizing the free radical-induced oxidative damage. Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR) and glutathione transferase (GST) constitute a major supportive team of defense against free radicals [67]. Targeting and modulating these physiological defense mechanisms by chemopreventive agents has become a part of many therapeutic strategies [68]. Also, one of the most important intracellular antioxidant systems is glutathione (GSH) which is essential for maintaining cell integrity by its reducing properties and participation in the cell metabolism [42].

It is obvious from the present results that, there was a differential response of the antioxidant enzymes to PD-injection. Interestingly, the results showed that, GSH content, CAT activity significantly decreased while SOD activity was not significantly changed after 2 and 14 days of kidney damage by PD, as compared with the normal control group. Chromate has a pro-oxidant effect, which was indicated by decrease of reduced glutathione (GSH) levels in different tissues [69]. Earlier studies have revealed that, chromium administration results in increased ROS production. To counteract the ROS production, the cell tend to increase intracellular GPx levels, which in turn might be responsible for the observed fall in GSH levels. Moreover, H$_2$O$_2$ is a free radical essentially responsible for the kidney damaging effect caused by administration of Cr and might be attributed to the decrease in CAT activity [70]. However SOD enzyme is localized even in the damaged epithelial tubular cells, the main site where Cr exerts its kidney damaging effect through the production of free radicals other than superoxide radical (O$_2^-$) [71]. The pre-treatment of animals with green tea and its combination with lycopene significantly increased GSH content, CAT activity while lycopene increased GSH and did not significantly change the CAT activity after 2 and 14 days of induction, as compared with the kidney damaged animals. These results might reflect the usefulness of green tea and lycopene, as excellent sources of antioxidants might directly be related to enhanced biosynthesis of GSH and increased levels of other antioxidants such as vitamin A, vitamin E [72] and the ability of green tea but not lycopene to counteract H$_2$O$_2$ which is one of the active oxygen species responsible for the oxidative stress produced in the damaged kidney by PD.

CONCLUSION

We conclude that green tea extract alone or with lycopene modulates glomerular, tubular and oxidative kidney damage and might have protective effect against potassium dichromate-induced ARF in rat more than lycopene alone.

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