Lycopene attenuates oxidative stress, apoptosis, and biochemical fluctuations induced by bisphenol A in the kidney of rats

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SUMMARY

Bisphenol A (BPA) is an environmental pollutant that harms different body systems. Previous investigations indicated that BPA exposure is linked to renal dysfunction. Among carotenoids, lycopene (Lyc) is one of the strongest antioxidants. This work was conducted to assess the potential protective benefits of Lyc on oxidative stress and biochemical and histological abnormalities induced by BPA in the kidney. Adult male rats were divided into: control group, Lyc group (4 mg/kg /day), BPA group (50 mg/kg/day), and Lyc-BPA group. The agents were given orally for eight weeks.

BPA induced a marked increment in malondialdehyde (MDA) and a marked decrement in the superoxide dismutase (SOD) level. A marked rise in creatinine and urea levels was also reported. Marked histopathological alterations were demonstrated in the renal cortex. Atrophy of the renal corpuscles, dilated tubules with degenerated epithelium, dilated congested cortical renal blood vessels, and cellular infiltration were demonstrated. Up-regulation of the immune expression of desmin and down-regulation of Bcl2 were also detected. Interestingly, co-administration of Lyc and BPA ameliorated to a great extent most of the biochemical and histopathological alterations induced by BPA. In conclusion, BPA had a harmful impact on the kidney of rats and Lyc protected against renal damage through its antioxidant, anti-inflammatory, and anti-apoptotic effects.

Key words: Bcl2 – Desmin – Creatinine – Urea – Oxidative stress

INTRODUCTION

Bisphenol A (BPA), an environmental hazard, is an extensively manufactured chemical (Eweda et al., 2020). BPA is primarily utilized as an epoxy resin precursor and a monomer in creating polycarbonate plastics. Polycarbonate plastics are used in beverage and food containers, and the resins are used to cover metal items such as water supply pipes, bottle caps, and cans. Additionally, BPA is utilized to create thermal paper, flame retardants, various resins, and polyvinyl chloride plastic manufacturing (Haroun et al., 2019). BPA-containing items are widely used, leading to extensive global human exposure (Vandenberg et al., 2010). Although inhalation and transder-

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mal absorption are potential additional exposure pathways, especially for individuals who work in organizations that make BPA-based goods, ingestion is the most common route of BPA exposure. (Kang et al., 2006, Zalko et al., 2011).

BPA is an endocrine disruptor that mimics estrogen and thyroid hormones (Eweda et al., 2020). Experiments employing laboratory animals and cultured cells revealed that BPA could accumulate and interfere with various essential organ activities, such as the pancreas, brain, liver, heart, and testis (Kobroob et al., 2018). Human epidemiological research implies a link between high BPA levels in urine and the possibility of hypertension or albuminuria (Moreno-Gómez-Toledano et al., 2022). Additionally, (Olea-Herrero et al., 2014) reported high urinary excretion of albumin and podocytopathy after five weeks of exposure to BPA. Saura et al. (2014) also reported that exposure to BPA was linked to hypertension in mice. Such results raised concerns about the likelihood that routine BPA exposure might harm the kidney and contribute to cumulative renal impairment, which worsens over time.

The principal carotenoid, lycopene (Lyc), is a fat-soluble red pigment in tomatoes, pink grapefruit, papaya, and watermelon (Stojiljković et al., 2020). Lyc has recently attracted special attention as the most potent antioxidant among carotenoids (Rao and Agarwal, 2000). It was stated that utilization of Lyc reduced oxidative injury to biological molecules like proteins, DNA, and lipids (Palabiyik et al., 2013). Additionally, previous research revealed that Lyc had anti-inflammatory properties. Lyc slowed the aging process and offered protection from various diseases, including heart diseases, Alzheimer's disease, and other malignancies (Kaya et al., 2015).

A beneficial relationship has been established between dietary antioxidant supplementation and the decrement of harmful impacts of numerous environmental and toxicant factors (Pandir et al., 2016). In view of the aforementioned medicinal qualities of Lyc, this experimental work was conducted to assess the potential protective benefits of Lyc on oxidative stress and toxicity caused by BPA-induced biochemical and histological alterations in the kidney.

MATERIALS AND METHODS

Animals

This investigation employed 40 mature male albino rats (190 ± 20 g). The animals were kept in three-animal polypropylene rat cages. The rats were acclimatized to regular laboratory settings for at least seven days before treatment, with temperatures ranging from 25 ± 2°C and 30-70% relative humidity and a 12/12-hour light-dark cycle. Animals ate experimental rat pellets and drank purified water. The research was done following the Laboratory Animal Care and Use Guide, and during the light phase (National Institute of Health Publication No. 80– 23, revised 1996).

Chemicals

Sigma Chemical Company supplied BPA powder (CAS register no. 239658) (St. Louis, MO), and Puritan's Pride, INC, USA supplied Lyc with 20 mg capsules.

Study protocol

Four groups of 10 rats each were assigned:

Group I (Control group) was then divided into subgroup (I), which was kept untreated, and subgroup (II), which was given 0.5 mL of corn oil, the diluting vehicle for Lyc and BPA; group II (Lyc group) was dosed with Lyc of 4 mg/kg /day (Pandir et al., 2016); group III (BPA group) received BPA at a dose of 50 mg/kg/day (Amin et al., 2023), and group IV (Lyc-BPA group) was given both Lyc and BPA as in previous groups. All preceding treatments were supplied orally by gavage as a single, newly generated daily dose for eight weeks.

After the investigation, the animals were sacrificed under ethyl ether anesthesia (Shalaby et al., 2019). Blood samples were taken through a heart puncture and coagulated at room temperature. After centrifuging the samples at 3000 rpm for 15 minutes, the separated sera were frozen at -20 C for future urea and creatinine biochemical analysis. After opening the abdominal wall, both kidneys were taken out, cleaned with cold saline, dried with filter paper and weighed. The right kidneys were kept at -80 degrees Celsius in liquid nitrogen until tissue homogenates were made. The

left kidneys were immersed in 10% buffered formalin for histological evaluation.

Biochemical analysis

Creatinine and urea levels in blood were determined using commercial kits from the French company Biolabo.

Assessment of oxidative stress

Superoxide dismutase (SOD) and malondialdehyde (MDA) levels were measured in kidney homogenates according to Marklund and Marklund (1974) and Uchiyama and Mihara (1978), respectively.

Light microscopic studies

The left kidney of each animal was divided lengthwise into two halves, fixed in a 10% buffered formalin solution for 24 hours, dried in increasing strength ethanol, and then embedded in paraffin. The following procedures were applied to serial sections of 5 µm thickness:

- Hematoxylin and Eosin (H&E) stain: to highlight the major histological characteristics.
- Periodic acid-Schiff (PAS) stain: to show the brush border and basement membrane of the proximal and distal convoluted tubules and the parietal layer of the Bowman's capsule (Layton and Bancroft, 2013).
- Immunohistochemical staining with the streptavidin-biotin-peroxidase method as described by Shalaby et al., (2020b), Shalaby et al., (2020a).

The slides were dewaxed and then treated in PBS with 3% H2O2 to quell any remaining endogenous peroxidase activity. After each procedure, PBS was used to clean up any residue (Alabiad et al., 2021a, Khayal et al., 2022). Antigenic retrieval of proteins required 15 minutes at 95 degrees Celsius in sodium citrate solution (10 mM, pH 6.0) (Alabiad et al., 2021b, Ahmed et al., 2021). Non-specific staining was prevented by incubating the slides in 10% normal goat serum in PBS for one hour at room temperature. Next, the slides were incubated with diluted primary antibodies, a mouse monoclonal antibody against desmin (cat # M 0760, Dako, Carpentaria California, USA) at a dilution of 1:100, and a mouse monoclonal antibody against Bcl2 (SC-7480, Dako, Carpentaria California, USA) at a dilution of 1:100, at 4 C overnight. The slides were treated with the appropriate biotinylated secondary antibody (Alabiad et al., 2021b, Elsalam et al., 2021). Then the slides were treated with the avidin-biotin combination. These immunopositive responses were induced by the addition of diaminobenzidine (DAB). Finally, Mayer's hematoxylin was applied to the sections as a counterstain.

Morphometric study

For image analysis, the "Image J version 1.47 software", National Institute of Health Bethesda, Maryland, USA (Tawfeek et al., 2021, Khayal et al., 2021), was utilized to measure the area percentages of desmin and Bcl2 expressions in the stained kidney sections immunohistochemically, as well as the area percentages of PAS-positive reaction.

Statistical Analysis

For each group, the morphometric data were displayed as mean ± SD. One-way analysis of variance (ANOVA) was used for statistical analysis, and $P < 0.05$ was used as the significance threshold for the post hoc Tukey test. The software Statistical Package for Social Sciences version 17 (SPSS Inc., Chicago, Illinois, USA) was used to analyze the data.

RESULTS

No deaths were observed among experimental rats.

Kidney weight results

The rats' kidney weight increased significantly ($p < 0.001$) after receiving BPA treatment compared to controls. Compared to rats given BPA alone, treatment with Lyc substantially decreased the higher kidney weight ($p < 0.001$) (Table 1).

Biochemical results

Comparing the BPA group to the control group, a substantial rise ($p < 0.001$) in the blood levels of urea and creatinine was observed, while Lyc treatment in the Lyc-BPA group significantly lowered their levels ($p < 0.001$) and succeeded in normalizing them (Table 1).

Oxidative stress results

The BPA group depicted a marked reduction in the SOD level and a marked rise in the MDA level versus the control group ($p < 0.001$). On the contrary, treatment with both Lyc and BPA significantly lowered MDA and elevated SOD compared with animals administrated BPA alone ($p < 0.001$) (Table 1).

Table 1. The effect of BPA, Lyc, Lyc-BPA combination on kidney weight, urea, creatinine, MDA, SOD, Area % of PAS, Area % of desmin, and optical density of Bcl2 levels in the kidney's rat.

	Control group (Group I)	Lyc group (Group II)	BPA group (Group III)	Lyc-BPA Group (Group IV)	ANOVA	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	F	P-value
Kidney weight (g)	1.52 ± 0.05	1.53 ± 0.09	2.53 ± 0.27	1.66 ± 0.05	55.037	<0.001*
Urea (mg dL– 1)	21.86 ± 1.21	22.48 ± 1.16	47.50 ± 1.77	23.56 ± 1.11	431.500	<0.001*
Creatinine (mg dL– 1)	0.74 ± 0.01	0.73 ± 0.03	2.15 ± 0.40	0.80 ± 0.01	60.076	<0.001*
MDA (mmol/mg tissue)	3.82 ± 0.34	3.62 ± 0.47	9.42 ± 1.18	4.09 ± 0.35	84.138	<0.001*
SOD (U/mg protein)	9.78 ± 0.35	10.01 ± 0.76	5.05 ± 0.45	9.06 ± 0.56	88.297	<0.001*
Area % of PAS	31.40 ± 2.30	30.40 ± 1.94	16.40 ± 1.14	29.39 ± 2.07	67.574	<0.001*
Area % of desmin	0.36 ± 0.03	0.35 ± 0.02	3.07 ± 0.50	0.44 ± 0.04	140.010	<0.001*
Optical density of Bcl2	0.86 ± 0.03	0.84 ± 0.02	0.57 ± 0.04	0.82 ± 0.02	130.683	<0.001*

TUKEY'S Test						
	I&II	I&III	I&IV	II&III	II&IV	III&IV
Kidney weight (g)	0.999	<0.001*	0.449	<0.001*	0.523	<0.001*
Urea (mg dL– 1)	0.883	<0.001*	0.227	<0.001*	0.592	<0.001*
Creatinine (mg dL– 1)	1.000	<0.001*	0.968	<0.001*	0.968	<0.001*
MDA (mmol/mg tissue)	0.967	<0.001*	0.916	<0.001*	0.692	<0.001*
SOD (U/mg protein)	0.911	<0.001*	0.202	<0.001*	0.063	<0.001*
Area % of PAS	0.842	<0.001*	0.381	<0.001*	0.842	<0.001*
Area % of desmin	1.000	<0.001*	0.966	<0.001*	0.961	<0.001*
Optical density of Bcl2	0.642	<0.001*	0.122	<0.001*	0.643	<0.001*

One-way ANOVA and Tukey's post-hoc test, n=5
* Indicates Significance.

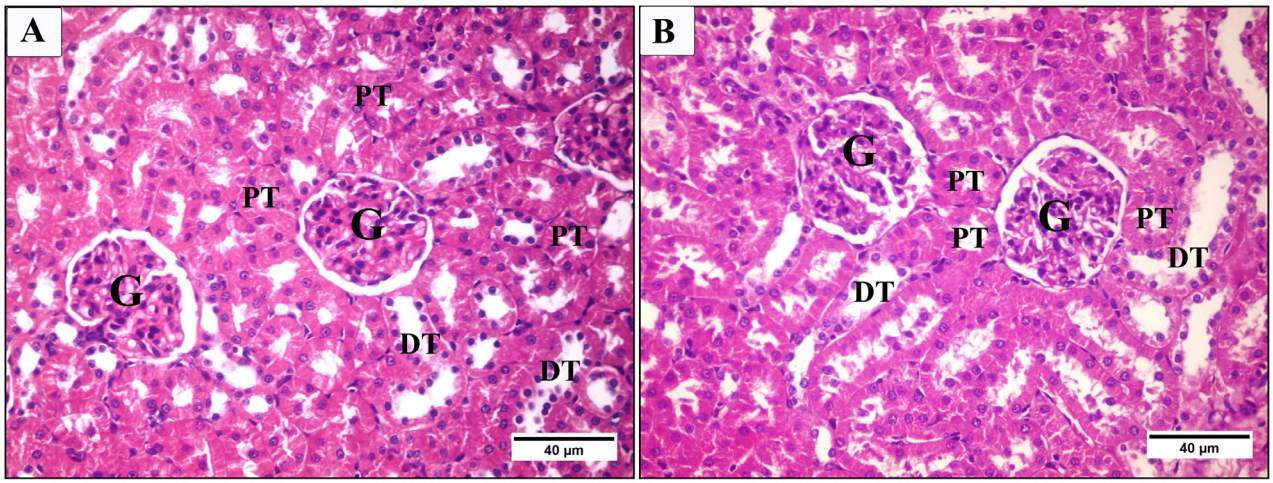

Fig. 1.- A: Control group and **B:** Lyc group showing normal glomeruli (G), distal convoluted tubules (DT), and proximal convoluted tubules (PT). (H&E ×400, scale bars = 40 µm).

Histopathological results

H&E-stained results

The control group and the Lyc group showed the normal structure of the renal cortex, which consisted of glomeruli, proximal convoluted tubules with deeply acidophilic cytoplasm and narrow lumen, and distal convoluted tubules with less acidophilic cytoplasm and a wider lumen (Fig. 1A, B). Administration of BPA for eight weeks induced changes in the renal cortex which included shrunken glomeruli and dilated tubules with atrophied epithelium and pyknotic nuclei (Fig. 2A). Dilated congested blood vessels, cellular infiltration, and edema between tubules were also detected (Fig. 2B, C), in addition to the presence of casts inside tubule (Fig. 2D). On the contrary, co-administration of both Lyc and BPA attenuated the histological alterations induced by BPA regarding glomeruli and tubules, as they appeared normal (Fig. 3A). Nevertheless, small foci of cellular infiltration were present (Fig. 3B).

PAS-stained results

A strong PAS-positive reaction was observed in the brush border of the tubules and in the basement membrane of the Bowman's capsule of the glomerulus and renal tubules in the control group and in the Lyc group (Fig. 4A, B), although the BPA group demonstrated loss of PAS-positive reaction in the brush border in most tubules with an ill-defined basement membrane (Fig. 4C). Regarding the Lyc-BPA group, it showed a strong PAS-positive reaction (Fig. 4D). The mean area fraction of PAS was found to be significantly decreased in the BPA group ($p < 0.001$) when compared to the control group. Contrarily, when Lyc and BPA were administered together, the mean area percentage of PAS was considerably higher ($p < 0.001$) than in the BPA group (Table 1).

Desmin immunohistochemistry results

Weak desmin expression within podocytes of the glomerulus was demonstrated in both the control and Lyc groups (Fig. 5A, B), whereas the

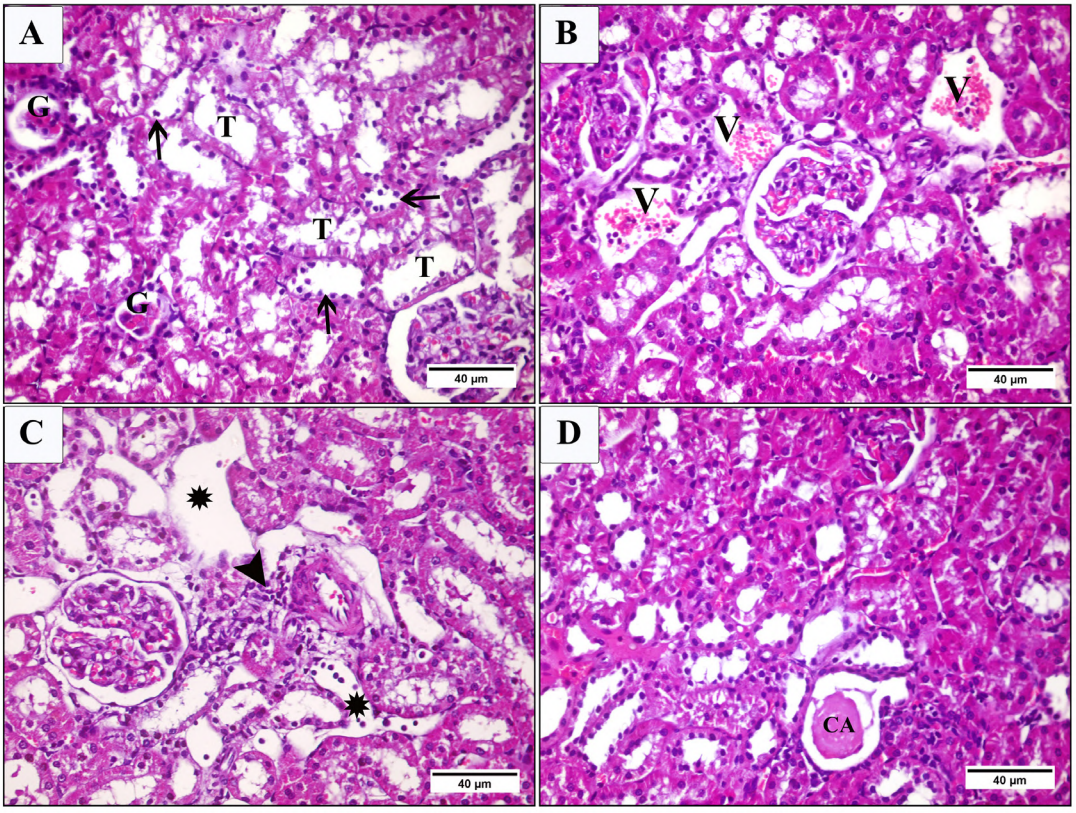

Fig. 2.- BPA group demonstrating: **A:** Shrunken glomeruli (G), dilated tubules (T) with atrophied epithelium and pyknotic nuclei (arrows); **B:** dilated congested blood vessels (V) in-between tubules; **C:** cellular infiltration (arrowhead) and edema (asterisks) in-between tubules; **D:** cast (C) inside tubule. (H&E ×400, scale bars = 40 µm).

BPA group demonstrated up-regulation of desmin expression (Fig. 5C). Regarding the Lyc-BPA group, IT displayed down-regulation of desmin expression (Fig. 5D). A significant increment ($p < 0.001$) in the mean area fraction of desmin expression in the BPA group in opposition to control group was reported. While administration of both Lyc and BPA significantly reduced ($p < 0.001$) the area fraction of desmin expression in opposition to the BPA group (Table 1).

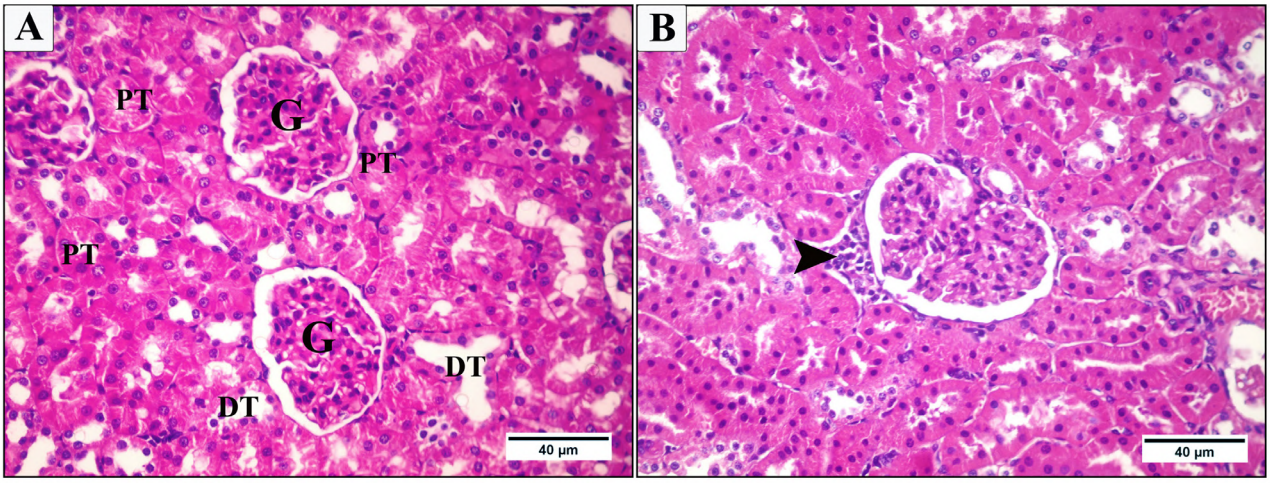

Fig. 3.- Lyc-BPA group demonstrating: **A:** normal glomeruli (G), distal convoluted tubules (DT), and proximal convoluted tubules (PT); **B:** a small focus of cellular infiltration (arrowhead). (H&E ×400, scale bars = 40 µm).

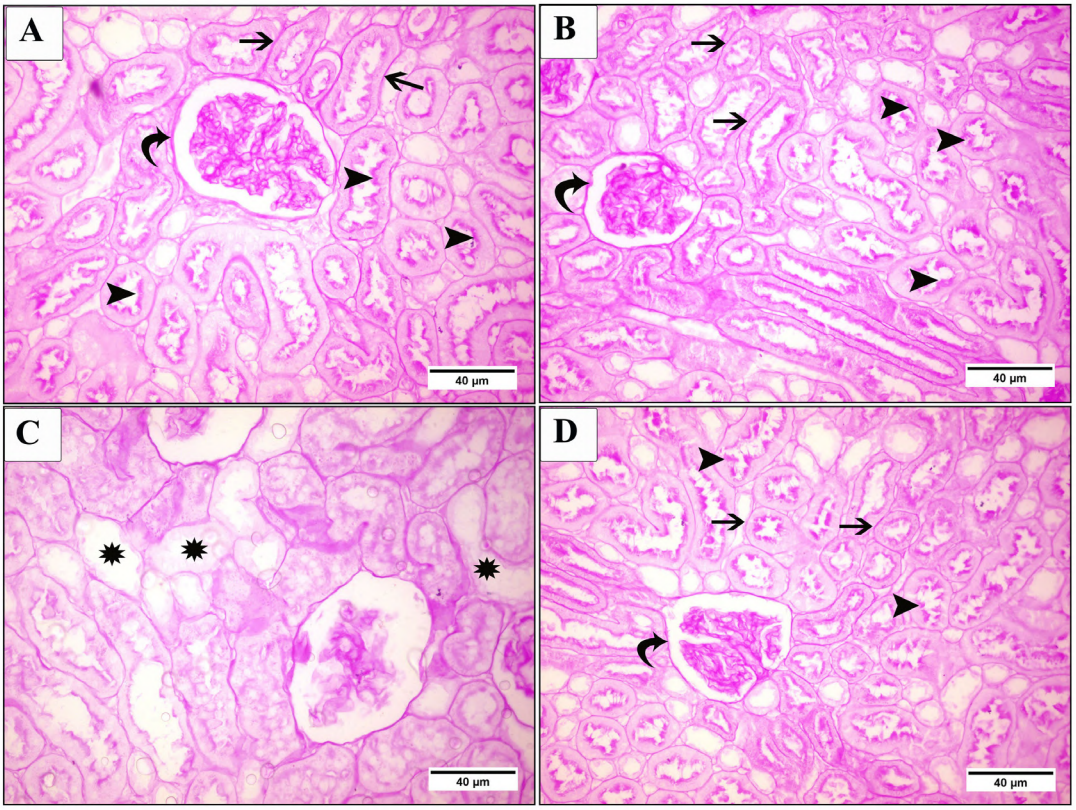

Fig. 4.- A: Control group and **B:** Lyc group demonstrating strong PAS positive reaction in brush border of tubules (arrowheads) and the basement membrane of Bowman capsule of glomerulus (curved arrow) and renal tubules (arrows). **C:** BPA group demonstrating; loss of PAS positive reaction in the brush border of tubules (asterisks) with ill-defined basement membrane. **D:** Lyc-BPA group revealing strong PAS positive reaction in brush border of tubules (arrowheads) and the basement membrane of Bowman capsule of glomerulus (curved arrow) and renal tubules (arrows). (PAS ×400, scale bars = 40 µm).

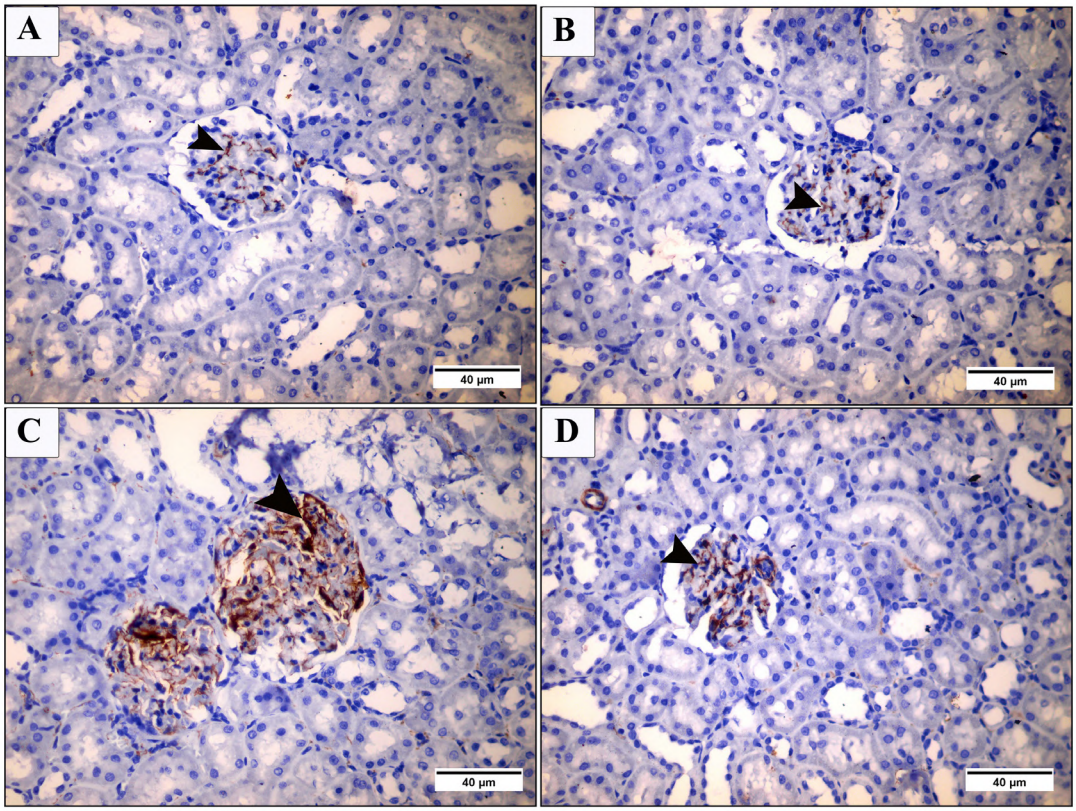

Fig. 5.- A: Control group and **B:** Lyc group revealing weak demin expression within podocytes of glomerulus (arrowhead). **C:** BPA group demonstrating; up-regulation of desmin expression (arrowhead). **D:** Lyc-BPA group displaying down-regulation of desmin expression (arrowhead). (Desmin immunostaining ×400, scale bars = 40 µm).

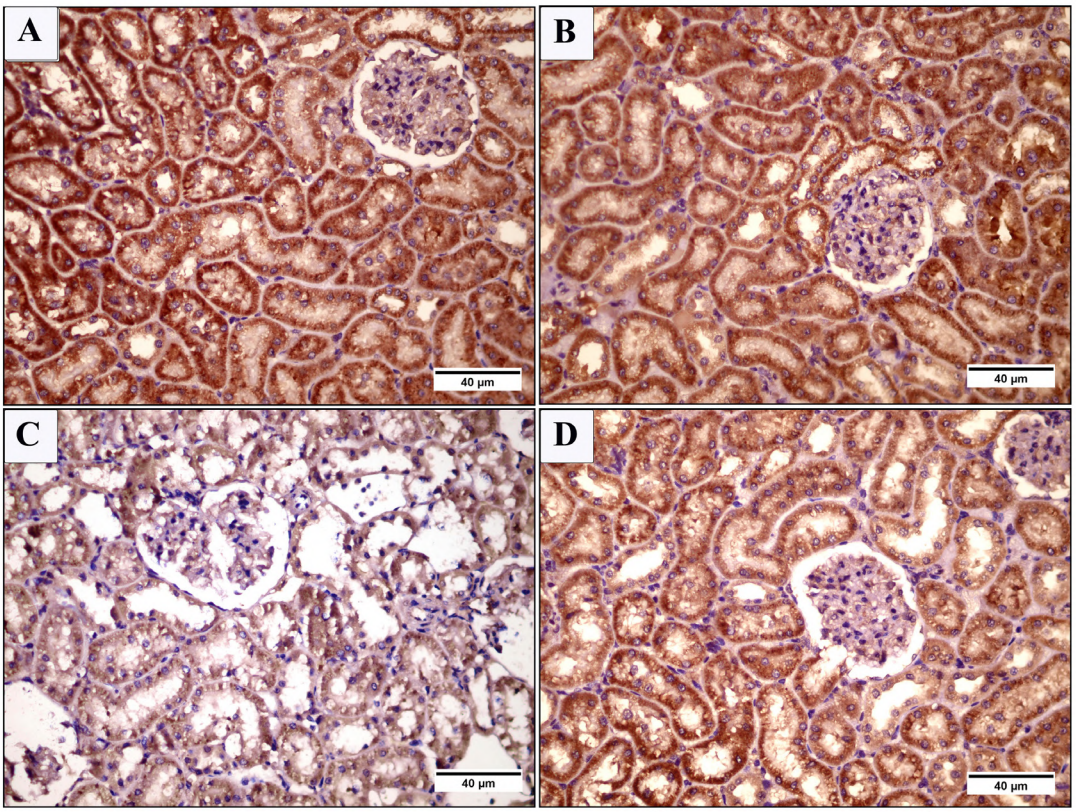

Fig. 6.- A: Control group and **B:** Lyc group demonstrating strong Bcl2 expression within glomerulus and tubules. **C:** BPA group demonstrating; down-regulation of Bcl2 expression. **D:** Lyc-BPA group displaying up-regulation of Bcl2 expression. (Bcl2 immunostaining ×400, scale bars = 40 µm).

Bcl2 immunohistochemistry results

Strong Bcl2 expression within the glomerulus and tubules was detected in both the control and Lyc groups (Fig. 6A, B). Down-regulation of Bcl2 expression was demonstrated in the BPA group (Fig. 6C). Up-regulation of Bcl2 expression was demonstrated in the Lyc-BPA group (Fig. 6D). The mean optical density of Bcl2 expression was significantly lower ($p < 0.001$) in the BPA group when compared to the control group. But when Lyc and BPA were administered together, the mean optical density of Bcl2 expression was considerably higher ($p < 0.001$) than in the BPA group (Table 1).

DISCUSSION

Concerns regarding the impact of BPA exposure on human health have lately been raised, since extensive exposure has been found among populations in numerous nations. (Björnsdotter et al., 2017). Because BPA is used in so many daily plastic items, it has the potential to drastically damage the environment, either by leaking from plastic water and food containers or as a consequence of manufacturing. As a result, the principal sources of exposure are food and drink. (Helal et al., 2013). The main goal of this investigation is to evaluate the efficacy of Lyc as a protecting agent against the renal impacts of BPA. The study's findings validate the effect of BPA on the kidney and provide new insight into the possible effective role of Lyc in mitigating the detrimental cellular consequences associated with BPA exposure.

The current research reported a marked increment in the weight of the kidney of rats that were administered BPA. This result coincided with Poormoosavi et al., (2018), who detected the same finding in their work on rats. They indicated that BPA is a xenoestrogen and could activate the estrogen receptors in the kidney, subsequently promoting the growth of epithelial cells. On the other side, BPA may result in hydronephrosis by increasing the volume of the renal tubules. The present work revealed that BPA deteriorated kidney functions, as confirmed by the significant rise in the serum levels of creatinine and urea. This was in harmony with Edres et al., (2018), who indicated comparable results in their investigation on rats that were administered BPA. The accumulation of BPA-toxic compounds in the kidney with the inability to remove them led to nephrotoxicity, with a subsequent rise in creatinine and urea levels (Wahby et al., 2017). Kobroob et al., (2018) also added that BPA damaged the kidney glomeruli with decreased glomerular filtration, which could explain impaired kidney function.

Regarding the influence of BPA on oxidative/antioxidative markers in rat kidney tissues, the current work depicted that BPA caused oxidative stress in the kidney of rats, as evidenced by the marked increase in MDA coupled with a marked reduction in the level of SOD. This finding was in agreement with Poormoosavi et al. (2018), who had comparable results in rats that were administered BPA. BPA was reported to increase reactive oxygen species (ROS) production (Asahi et al., 2010). In the same line, Morgan et al. (2014) discovered that BPA treatment caused lipid peroxidation in testicular, brain, and kidney tissue, as evidenced by considerably lower GSH concentrations and higher MDA levels. Furthermore, Eid et al. (2015) reported a reduction in antioxidant capacity and an increase in MDA levels after exposure to BPA. Additionally, patients using BPA-containing polysulfone dialysers had also been found to have high serum levels of BPA and elevated indicators of oxidative stress (Bosch-Panadero et al., 2016).

The analysis of the renal cortex histology of the current study in BPA-treated rats showed atrophied renal corpuscles, dilated tubules with degenerated epithelium, dilated congested cortical renal blood vessels, and infiltration of mononuclear cells. These findings were in harmony with the earlier work of Korkmaz et al. (2011) and Ahmed et al. (2015), who observed similar findings in the kidney of BPA-exposed rats. These changes could be attributed to oxidative damage caused by BPA (Kobayashi et al., 2020). It was stated that increased ROS levels by BPA caused mutations, accelerated cell proliferation, lipid peroxidation, DNA damage, mitochondrial malfunction, and protein alteration, all contributing to renal damage and inflammation (Priego et al., 2021).

According to in vitro research, BPA enhanced the generation of pro-inflammatory cytokines,

such as TNF-α and IL-6 (Lee and Lim, 2010). In a recent study conducted in rats, ingestion of BPA for four weeks increased pro-inflammatory cytokine generation and secretion, with a subsequent decrease in renal function (Alekhya Sita et al., 2019). Furthermore, mice exposed to BPA for a long time showed a rise in the amount of $CD3^+$ T lymphocytes in the interstitium of the kidney, which was more noticeable in damaged kidneys, leading to the generation and secretion of more inflammatory mediators (Priego et al., 2021).

Up-regulation of desmin expression was demonstrated in rats administered BPA in our research. Consistent with our results, Fadda et al. (2019) indicated that podocyte injury was enhanced in rats with a subsequent increase in desmin expression. Previously, increased desmin expression in podocytes was shown in various rat renal diseases, including diabetic nephropathy (Kakimoto et al., 2014). Desmin and vimentin, two intermediate filament proteins, are expressed in podocytes. Desmin is mostly detected in vascular smooth muscle and mesangial cells, with podocytes showing extremely faint expression (Zou et al., 2006). Thus, desmin expression is a reliable indicator of early podocyte damage (Gross et al., 2003).

The present work indicated that BPA induced apoptosis in the renal cortex, as confirmed by the marked decrease in Bcl2 expression. This finding was in agreement with Fadda et al. (2019), who demonstrated apoptosis in renal cells after exposure to BPA. In the same line, Peerapanyasut et al. (2019) indicated a significant increase in pro-apoptotic genes in the kidney after exposure to BPA. According to Bosch-Panadero et al. (2018), BPA promotes mitochondrial damage, oxidative stress, and apoptosis in renal tubules in a concentration-dependent manner. Moreover, Olea-Herrero et al. (2014) discovered that different concentrations of BPA could elicit podocyte death after nine days in culture using the tunnel assay.

The present investigation revealed that Lyc administration improved renal function and reduced the biochemical and histopathological changes caused by BPA in rats. The current study reported normalization of serum creatinine and urea levels in rats that were co-administered Lyc and BPA. This finding coincided with a prior work of Karahan et al. (2005), who indicated that Lyc treatment normalized serum creatinine and urea levels in nephrotoxicity caused by gentamicin. Also, Gori et al. (2021) indicated that Lyc treatment improved renal functions and lowered the high serum levels of urea and creatinine in adenine-induced renal damage in rats, and attributed this to improved glomerular filtration rate with subsequent enhancement of toxin metabolism.

A marked decline in the MDA level coupled with a rise in the SOD level in rats administrated both Lyc and BPA, suggesting the antioxidant effect of Lyc. In the same line, Hussein et al. (2018) indicated that Lyc treatment significantly increased kidney antioxidant enzymes in diabetic nephropathy in rats. Furthermore, Lyc treatment protected renal cells from lipid peroxidation caused by furan, the level of deceased MDA, and the increase in SOD (Pandir et al., 2016). Moreover, Lyc is an effective scavenger of free radicals and has a constant physical rate of quenching with ROS (Koul et al., 2010, Palabiyik et al., 2013).

The current investigation demonstrated that Lyc supplementation attenuated the histopathological changes caused by BPA. According to Pandir et al.(2016), Lyc could prevent furan-induced oxidative damage to the rat kidney by enhancing renal function, minimizing histopathologic alterations, lowering MDA generation, and restoring antioxidant enzyme activities. Additionally, a prior study by Yilmaz et al.(2006) found that Lyc prevented the kidney alterations brought on by adriamycin, and they attributed this result to the antioxidant capabilities of Lyc. Numerous investigations also discovered that it protects against chemically induced kidney injury (Aydin et al., 2013, Palabiyik et al., 2013). Moreover, Lyc drastically reduced the generation of inflammatory cytokines in rats with diabetic nephropathy (Tabrez et al., 2015). The suppression of pro-inflammatory cytokine synthesis and secretion and modification of signal transduction pathways could explain the anti-inflammatory effect of Lyc (Palozza et al., 2010).

Down-regulation of desmin expression was demonstrated in rats that were co-administered Lyc and BPA. El-Gerbed (2014) indicated that Lyc treatment improved alterations in the podocyte

foot process and protected podocytes. These data corroborate our findings. In our investigation, co-administration of both Lyc and BPA caused up-regulation of Bcl2 immune expression. This was consistent with the earlier study that concluded that Lyc reduces apoptosis (Buyuklu et al., 2015). Lyc administration significantly enhanced the anti-apoptotic gene Bcl-2 and reduced pro-apoptotic gene levels in rats treated with cisplatin, suggesting that Lyc had anti-apoptotic effects (Dogukan et al., 2011).

CONCLUSION

Lycopene (Lyc), which had been shown to have antioxidant, anti-apoptotic, and anti-inflammatory properties, lessened BPA-induced kidney damage. The use of Lyc supplements as a natural nephroprotective component is recommended, as humans consume Lyc in large amounts through goods such as tomatoes, tomato sauce, watermelons, melons, and grapefruits.

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