Original Article

Harmful Impacts of Bisphenol A on the Prostate of Adult Albino Rat and the Possible Role of Recovery: Histological and Immunohistochemical study

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ABSTRACT

Introduction: Huge amounts of bisphenol A (BPA) are manufactured all over the world. The prostate is the major accessory sex gland of mammalian males. BPA can be toxic to prostatic tissues.

Objectives: Investigate the impact of BPA on the prostate gland of adult male albino rats and the possibility of recovery.

Materials and Methods: Thirty adult male albino rats (180-220 g) were assigned into three groups. Control group: received 1mL of corn oil via gavage once daily for 8 weeks; BPA group: given 50 mg/kg of BPA in 1mL corn oil orally/ day for 8 weeks; Recovery group: given BPA the same manner as in BPA group and held without treatment for another 4 weeks. At the end of the study, blood was collected to measure serum testosterone. The prostate gland was removed and prepared for histological and immunohistochemical analysis.

Results: In the BPA group, the testosterone level dropped significantly. Irregularity of prostatic acini; thickening, and hyperplasia of the prostatic epithelium; abundant stroma with congested blood vessels were seen in hematoxylin and eosin (H&E)-stained sections. Morphometry revealed that the epithelial height, number of proliferating cell nuclear antigen (PCNA) positive cells, and the area percentage of collagen were significantly higher while the acinar surface area, acinar perimeter, and the optical density (OD) of androgen receptors (AR) in epithelial cells were significantly lower. These changes partially resolved after stopping BPA treatment.

Conclusion: The Prostate gland of adult rats can partially recover from the harmful impacts of bisphenol A.

Key Words: Androgen receptors, bisphenol A, PCNA, prostate, recovery.

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INTRODUCTION

All over the world, huge amounts of bisphenol A (BPA) are manufactured to be used in various life facilities. Daily life plastic products such as water bottles, bags, and kitchen tools account for the main and most serious source of food contamination with BPA. Other roots of BPA exposure include inhalation and transdermal absorption[1,2].

Bisphenol A is an endocrine disruptor chemical (EDC) that can produce hormonal imbalance by interference with nuclear receptors.[3] In humans, epidemiological studies have correlated exposure to BPA with reproductive and hormonal problems along with perinatal, childhood and pubertal developmental adverse outcomes. As well, animal, and experimental studies have proven that BPA can be toxic to many organs including prostatic tissues[4, 5]. More recently, BPA has been regarded as a mutagenic and carcinogenic chemical[6].

Receptor's pathways interruption, enzyme inactivation, neuroendocrine dysfunction, modulation of immunological and inflammatory reactions, genotoxicity, and epigenetic effect mediate multi-organ toxicity induced by bisphenol[7].

The prostate is the major accessory sex gland of mammalian males that largely influences men's health[8]. Prostatic secretion, rich in zinc and kallikreins, is an essential component of seminal plasma mixture that plays a central role in sperm activation and capacitation and consequently male fertility[9].

The exogenous estrogenic properties of BPA worsen testosterone-induced benign prostatic hyperplasia in rats[10] and promote the proliferation of ventral prostate (VP)[11]. Moreover, BPA stimulated the proliferation of cultured ventral prostatic epithelial cells[12]. Light and electron microscopic destructive changes were observed in the reproductive organs such as prostate and seminal vesicles in rats treated with bisphenol A[13].

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Recovery from the deleterious effects of 0.05 mg/kg and 5 mg/kg of BPA on the sperm count, sperm motility, sperm viability, and expression of occludin was possible after stopping BPA treatment[14].

Consequently, this study aimed at investigating the changes that occur in the prostate gland of adult rats after treatment with bisphenol A and the possibility of recovery.

MATERIALS AND METHODS

Chemicals:

Bisphenol A (Sigma–Aldrich Inc, Germany) in the form of white powder.

Animals and study groups:

Thirty adult male albino rats (180-220 g) purchased from animal house and laboratories faculty of medicine; Zagazig University were assigned for this experiment. The rats were allowed to acclimatize for 7 days before the beginning of the experiment. Ten rats were chosen randomly as a control (vehicle) group in which the rats received 1ml of corn oil via gastric tube for 8 weeks. The remaining rats were treated for 8 weeks with 50 mg/kg of BPA[15] dissolved in 1ml corn oil through gavage as a daily oral dose[16] and furtherly subdivided into BPA group (10 rats), sacrificed 8 weeks after the start of BPA treatment and recovery group (10 rats) kept without any treatment for another 4 weeks. All animals were housed in separate cages in an air-conditioned room (temperature 23-27 Ċ and 40-60% humidity) with 12h. light/12h. dark cycle. Throughout the experiment, rats were fed a standard diet and permitted water ad libtium. Glass containers were used to provide water to avoid the contamination with BPA. At the end of the experiment, the rats were anesthetized using intraperitoneal injection of thiopental 50 mg/kg and the prostate dorsolateral lobe were removed and processed for histological and immunohistochemical study. The protocol of the study and all the experimental procedures were performed in accordance with Zagazg University Institutional Animal Care and Use Committee (ZU-IACUC/3/F/24/2021).

Biochemical study:

Blood samples from the studied groups were withdrawn from the retro-orbital plexuses using micro-capillary tube. Serum testosterone hormone assay was done by Enzyme-Linked Immuno-Sorbent Assay (ELIZA) kits (IB79174, IBL-America, Minne-apolis, Minnesota, USA) as described by Finley and Tietz[17].

Histopathological and immunohistochemical studies for light microscopy

Prostate glands were fixed with 4% paraformaldehyde in 0.1M phosphate buffer overnight at 4 °C. After fixation, prostate specimens were dehydrated in graded ethanol, embedded in paraffin, and sectioned to obtain paraffin sections (3µm-thick). Then the sections were deparaffinized and hydrated, followed by staining with hematoxylin and eosin (H&E) for routine histological analysis and Masson's trichome stain for detection of collagen distribution.[18]

For immunohistochemical analysis, as described by Leong *et al*.[19], the deparaffinized and hydrated 3-4 sections of the prostate were incubated in citrate buffer (pH 6.0) for 20 min at 105 °C to distinguish androgen receptors (AR) and proliferating cell nuclear antigen (PCNA) positive cells. The sections were incubated at 4°C for 30 min in absolute methanol comprising 0.3% H2O2 to block endogenous peroxidase activity, afterward washed with water and incubated with 10% normal serum (donkey serum for PCNA staining and goat serum for staining of AR antigen) for one hour at room temperature. Sections were then incubated overnight with the primary antibody dilutions: goat polyclonal anti-PCNA (1:2000; sc9857, Santa Cruz, Biotechnology INC, Europe) and rabbit polyclonal anti-AR (N-20, sc-816; Santa Cruz Biotechnology, Inc., Santa Cruz, CA) diluted 1:100 in 1% BSA in PBS. The segments were washed with PBS three times (5 min each), taken after that for brooding with a biotin-conjugated secondary counteracting agent (goat anti-rabbit IgG) for staining the antigen-antibody complexes. To reveal non-specific binding, negative control was done by omitting the primary antibodies.

Photographs were captured using LeicaICC50W light electric microscope at the Image Analysis Unit of Anatomy and Embryology Department, Faculty of Medicine, Zagazig University.

Morphometric analysis

Morphometric analysis was performed using ImageJ (FIJI) software by examining 10 histological fields per section of the prostate gland from 5 different rats randomly chosen in each group[20].

In hematoxylin and eosin-stained slides, epithelial height was measured in µm by a line extending perpendicularly from the basement membrane to the top of the epithelial lining using X400 magnification. Acinar perimeter and acinar surface area were measured in µm and µm2 respectively by tracing the prostatic acini in fields with X100 magnification.

The amount of collagen in the prostate stroma was expressed as the area percentage of greenish color according to the method described by Chen *et al*.[21].

PCNA score was used to evaluate PCNA immunostaining. It was calculated by dividing the number of PCNA positive cells (cells with obviously brown-stained nuclei) by the total number of cells in each field[22].

To demonstrate androgen receptor immunoreactivity, the OD of staining intensity of AR was measured in the nuclei of prostatic epithelial cells[23].

STATISTICAL ANALYSIS

Continuous variables are quantified as the mean ± SD as the data showed normal distributions (parametric). We used one-way ANOVA to observe significant differences between groups. Post hoc Tukey's test was carried out for several comparisons between groups. The differences were significant at $P < 0.05$. All statistical comparisons were two tailed. All statistical calculations were done using GraphPad Prism software, version 8.0.2 (GraphPad Software, San Diego, CA, USA).

RESULTS

Biochemical results

Testosterone level in the sera of control rats was in average (3.914 ± 0.423). In the BPA group, there was a significant decline (2.188 ± 0.58, $P <0.0001$). Sopping treatment with BPA for 4 weeks significantly elevated testosterone level that was insignificantly lower than in the control group (2.697 ± 0.338) (Fig.1).

Histopathological results

Hematoxylin and eosin stain examination of the control group revealed that the dorsolateral prostate (DLP) had regular size acini with minimal infoldings and eosinophilic prostatic secretions in their lumina. The acini were separated by scanty connective tissue stroma (Fig.2a, b). On higher magnification, the acini were lined with simple cuboidal cells with central dark nuclei that had infrequent supranuclear cytoplasmic pallor. A delicate layer of fibromuscular stroma surrounds the acini that contained blood vessels (Fig.2c). On the contrary, in the BPA treated group, the prostatic acini appeared irregular and disorganized with empty cavities or containing pale scares secretions. Sloughed epithelium was observed in the lumen of some acini. Thickened lining epithelium, frequent infoldings, and hyperplasia infiltrating the interstitial space with areas of degeneration were also noticed. The stroma contained an abundant amount of connective tissue and markedly congested blood vessels (Figs.3a-e). However, in the recovery group, most acini were lined by simple columnar epithelium with basal dark rounded nuclei, others still had area of epithelial thickening. The fibromuscular layer around the acini was reduced. The blood vessels were less congested (Figs. 4a, 4b).

Masson's trichome stain results:

The prostate sections of control group stained with Masson's trichrome showed thin layer of collagen fibers in between the adjoining prostatic acini. (Fig. 5a). Dense bundles of collagen fibers were detected between the acini in the treated group (Fig. 5b). In the recovery group prostate sections showed less collagen fibers deposition in the inter-acinar spaces compared to treated group (Fig. 5c). These results confirmed morphometrically and statistically by measuring the area percent of the collagen staining (Fig.5d).

Immunohistochemical expression and quantification results:

PCNA immunostaining

Weak expression was observed in the lining epithelium in the control group (Fig. 6a). Prostate sections from rats in the BPA group showed strong expression especially in the areas of hyperplasia (Fig. 6b). In the recovery group there was weak to moderate staining. Using morphometrical analysis, there was a significant increase in the number of cells with anti-PCNA stained nuclei in relation to the total number of the cells in the same field (61.01± 9.08, $P <0.0001$) when compared with control rats (13.48 ± 6.01). PCNA score decreased significantly in the recovery group (34.55 ± 15.85, $P =0.006$) but was still statistically different from the control group (Fig. 6d).

AR immunoreactivity

The nuclear reaction of androgen receptors was detected in the nuclei of almost all prostatic epithelial cells of the control rats (Fig. 7a) meanwhile, the immunoreactivity in BPA group was less intense especially in the hyperplastic areas (Fig. 7b). Expression in the recovery group was the same as in control (Fig. 7c). Regarding the OD of AR, the BPA treatment induced a borderline significant reduction in the OD of AR in the epithelium of prostatic acini when compared to rats that treated with vehicle only (0.233 ± 0.075 versus 0.284 ± 0.083, $P =0.048$). However, in the recovery group, the OD was not statistically different from the control group (Fig. 7d).

Morphometric results:

The mean epithelial height in the control group was 8.22±3.04 µm. In the BPA group height of lining epithelium significantly increased (21.36 ± 6.18, $P <0.0001$). In the recovery group, epithelia thickness showed a significant decline (17.12 ± 5.88, $P =0.034$), however still statistically

higher than control (*P <0.0001*) (Fig. 8a). On the other hand, the surface area and perimeter of prostatic acini showed a significant reduction in the BPA group when compared with the control one (*P <0.0001*). Meanwhile, there was no statistical difference in these parameters between the recovery and control groups (Fig. 8b, c).

The results of Masson's trichrome satin were confirmed morphometrically and statistically by measuring the area percent of the collagen staining where the mean area percentage of collagen was (6.01 ± 1.7) in the control rats. In the BPA group, the area occupied by collagen significantly increased (16.5 ± 3.65, *P <0.0001*) compared to the control group. In contrast, after stopping BPA administration, the area percentage of collagen was significantly lower than the BPA group (10.36 ± 2.71, *P =0.0047*) and barely significantly higher than the control group (*P= 0.042*) (Fig.5d).

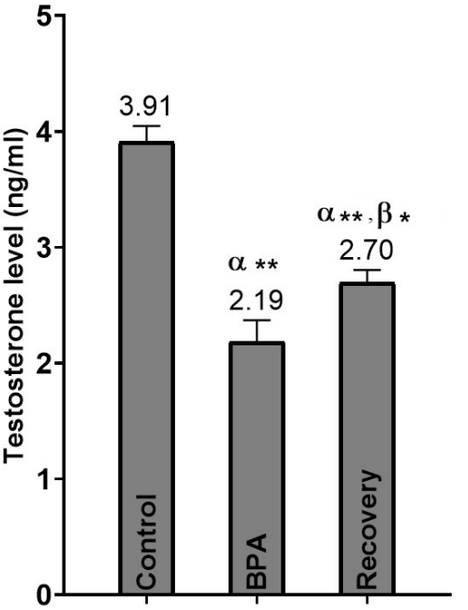

Fig. 1: Bar chart showing the testosterone level in the sera of the three studied groups. ** significant at level *p <0.0001*, * significant at level *p =0.049*. α versus control. β versus BPA.

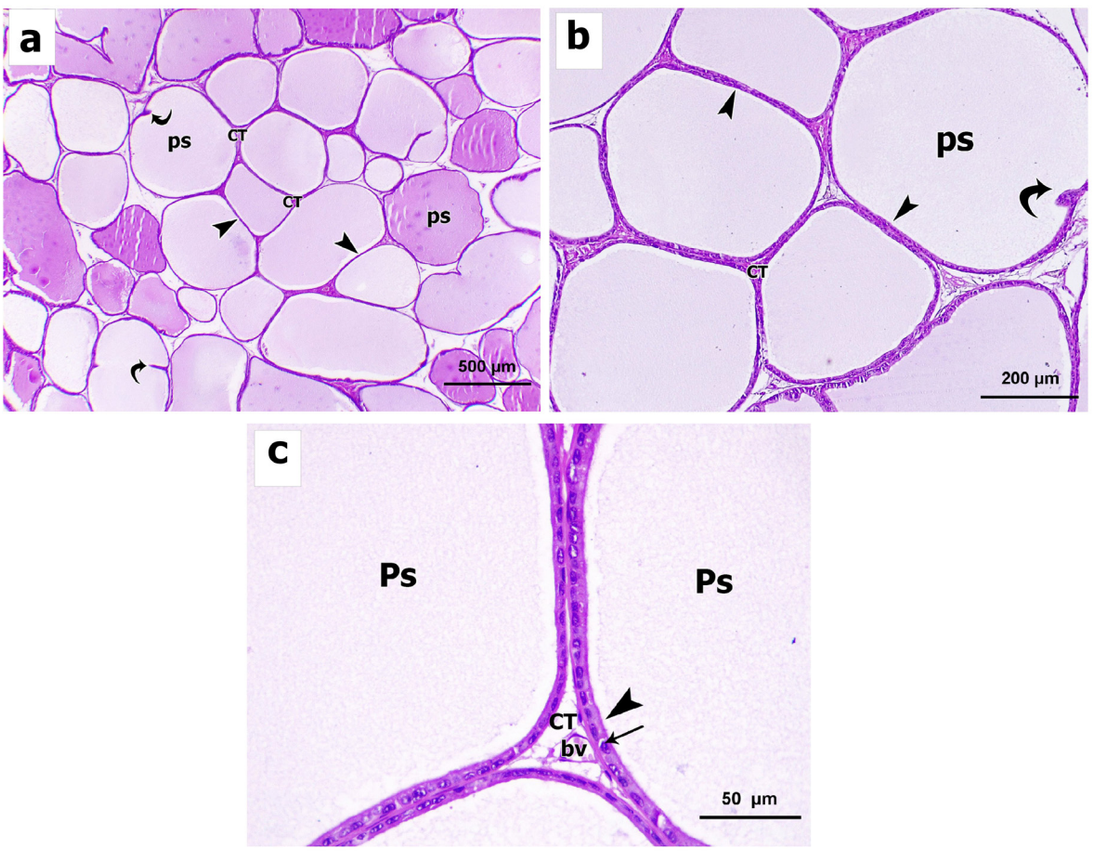

Fig. 2: Photomicrographs of a section in control adult albino rat prostate showing (a, b) regular acini with minimal epithelial infolding (curved arrow) containing acidophilic prostatic secretions (ps) in their lumen. The acini are surrounded by thin stroma (arrow heads) and separated by narrow connective tissue (CT). (c) A higher magnification image showing the acini lined with simple cuboidal epithelium with centrally located nuclei (arrowhead) and infrequent supranuclear pallor (arrow) embedded in a thin fibromuscular stroma. The interstitial space contains scanty amount of connective tissue (CT) and blood vessel (bv). (Hx & E, 2a: X40, scale bar =500 µm; 2b: X100, scale bar =200 µm; 2c: X400, scale bar =50 µm).

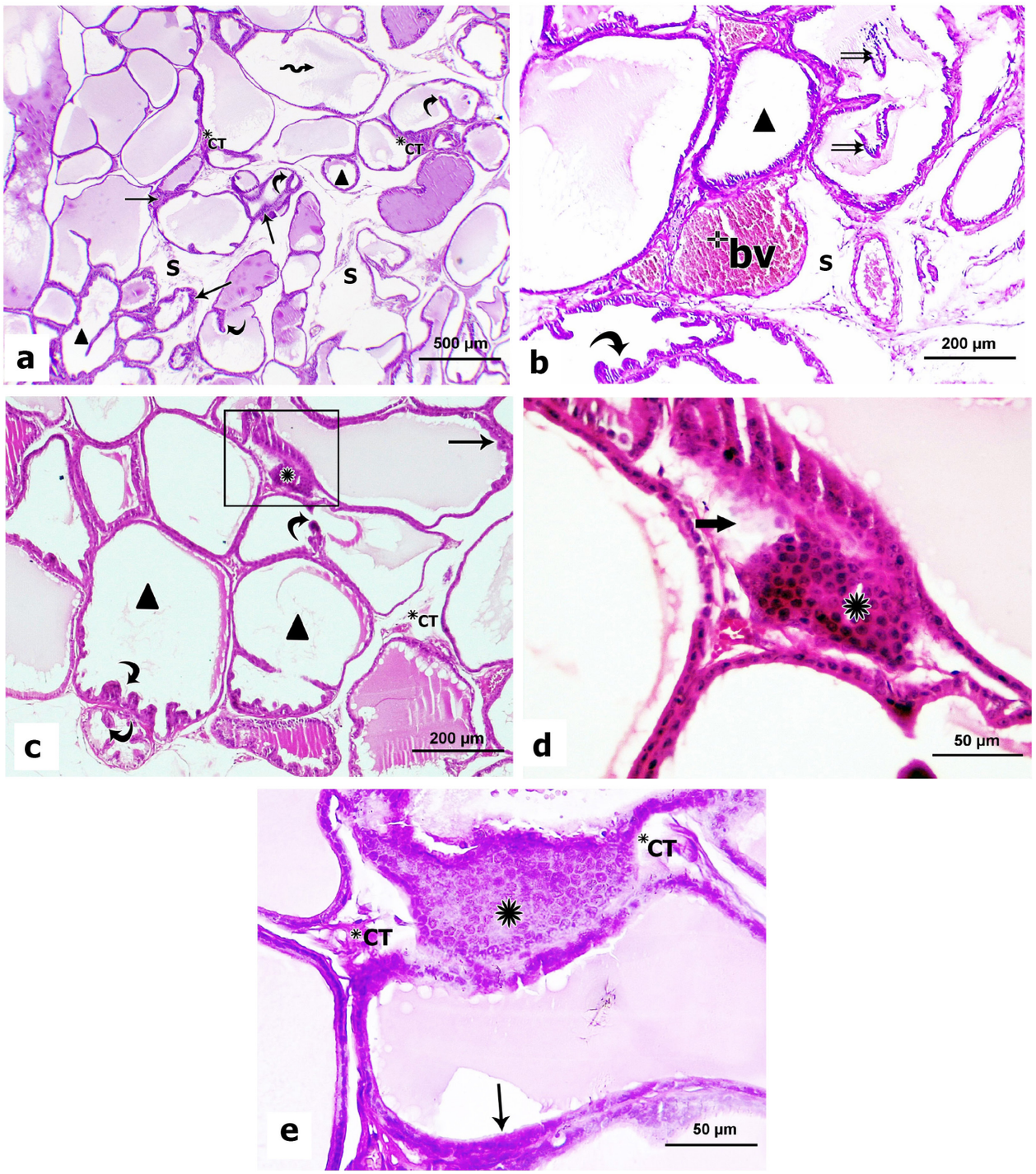

Fig. 3: Photomicrographs of sections in the prostate gland of adult albino rats in the BPA group showing: (a,b) Most of the acini are irregular and distorted, surrounded by loosely arranged stroma (S). Some acini have empty lumen (▲), others have scanty pale secretion (wavy arrow) and sloughed cells (double arrow). The epithelial lining shows area of thickening (arrow) and frequent infoldings (curved arrow). The interstitial space contains abundant amount of connective tissue (*CT) and congested and dilated blood vessel (+bv). (c): showing disorganised acini of variable size; thickened epithelium (arrow); many papillary projections (curved arrows); marked hyperplasia (star) with area of degenerations (thick arrow); the interstitial space contains abundant amount of connective tissue (*CT). (d): a higher magnification of the square in the previous section. (e): showing another example of epithelial thickening (arrow) and epithelial hyperplasia (star) and wide interstitial space with disorganized connective tissue (*CT). (Hx & E, 3a: X40, scale bar =500 µm; 3b,c: X100, scale bar =200 µm; 3d,e: X400, scale bar =50 µm).

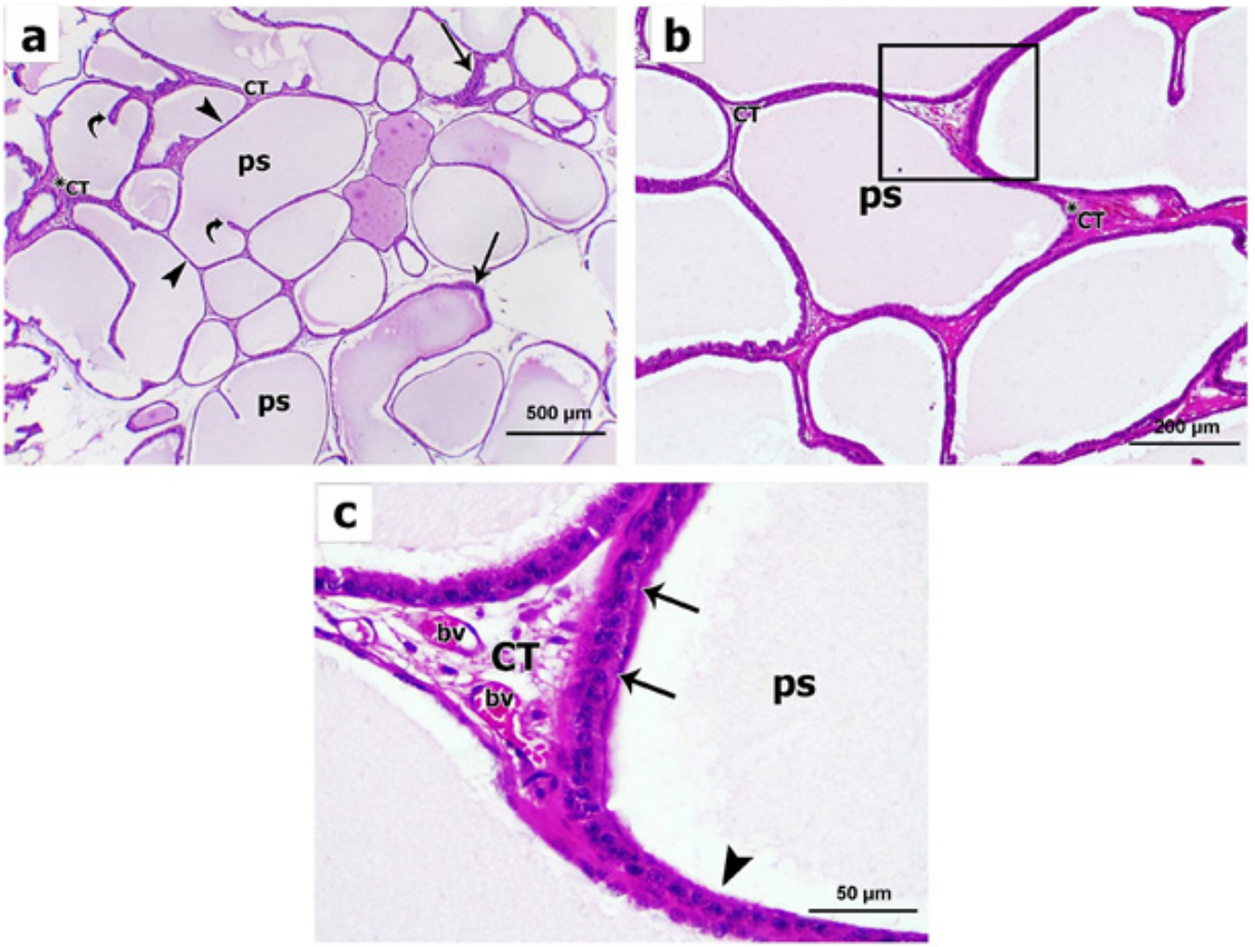

Fig. 4: photomicrographs of sections from adult albino rat's prostate gland in the recovery group showing: (a,b) Acini show more regularity; acidophilic secretions in the lumina of most acini (ps); few areas of epithelial thickening (arrow) and infoldings (curved arrow); thin stroma (arrowhead) containing scanty connective tissue (CT); however, the interstitial space in some areas contains thick connective tissue (*CT) with dilated blood vessel (bv). (c): A higher magnification showing slightly thick interstitial space with disorganized connective tissue (CT) and mildly congested blood vessels (bv); epithelium shows areas with normal thickness (arrowhead) and areas of thickening (arrow). (Hx & E, 4a: X40, scale bar =500 µm; 4b: X100, scale bar =200 µm; 4c: X400, scale bar =50 µm).

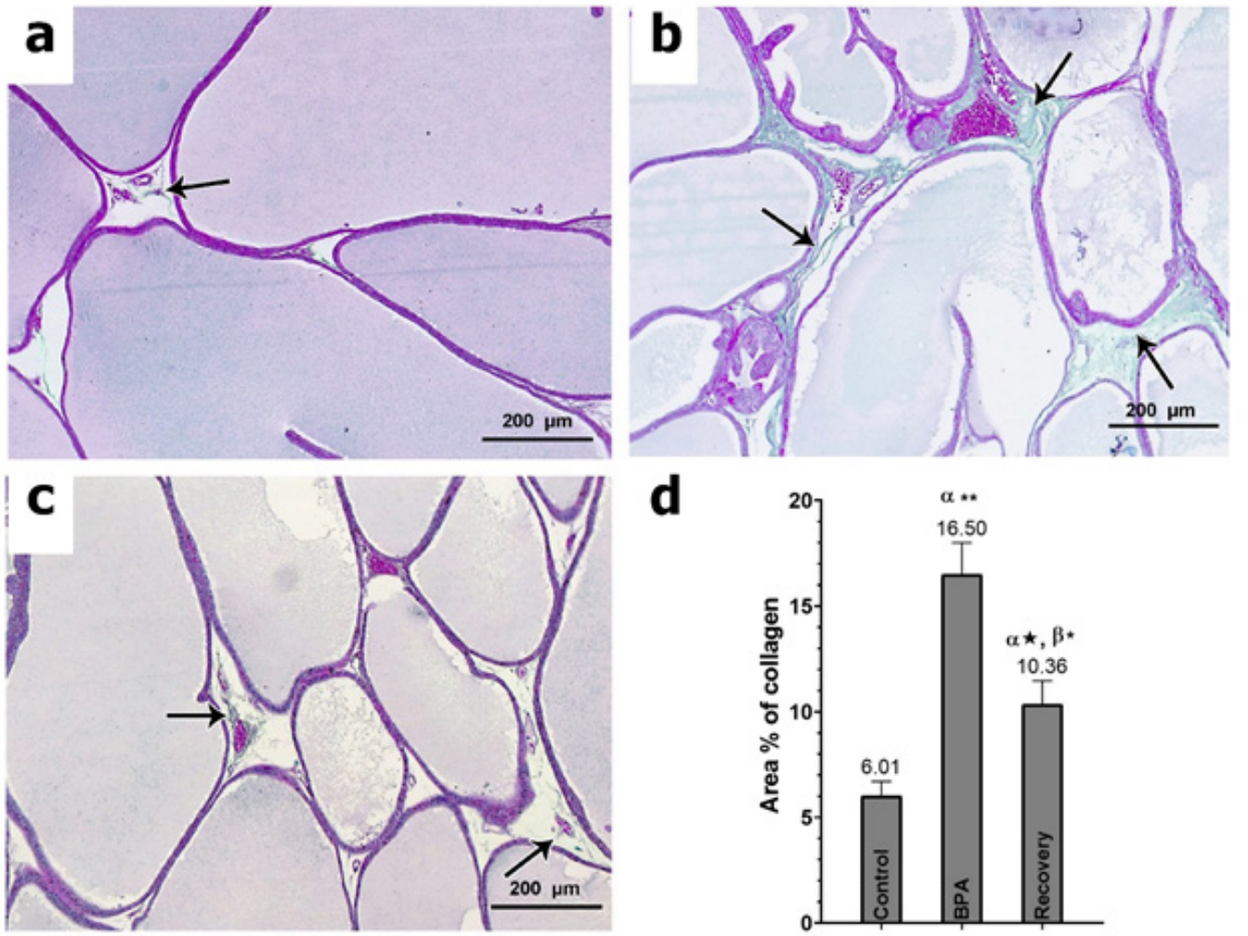

Fig. 5: Photomicrographs showing Masson's trichome stained sections in adult albino rat's prostate gland from the three studied groups. (a) Prostate of control rats, (b) Prostate of BA treated rats (c) Prostate of recovery rats. Arrows refer to the greenish staining of collagen fibres (Masson's trichrome, 1a, 1b, 1c: X100, scale bar =200 µm). (d) Bar chart showing the quantitative analysis of the area percentage of collagen fibres in prostatic sections from the three studied groups. ** significant at level $p < 0.0001$, * significant at level $p = 0.0047$, * significant at level $p = 0.0423$. α versus control. β versus BPA**.**

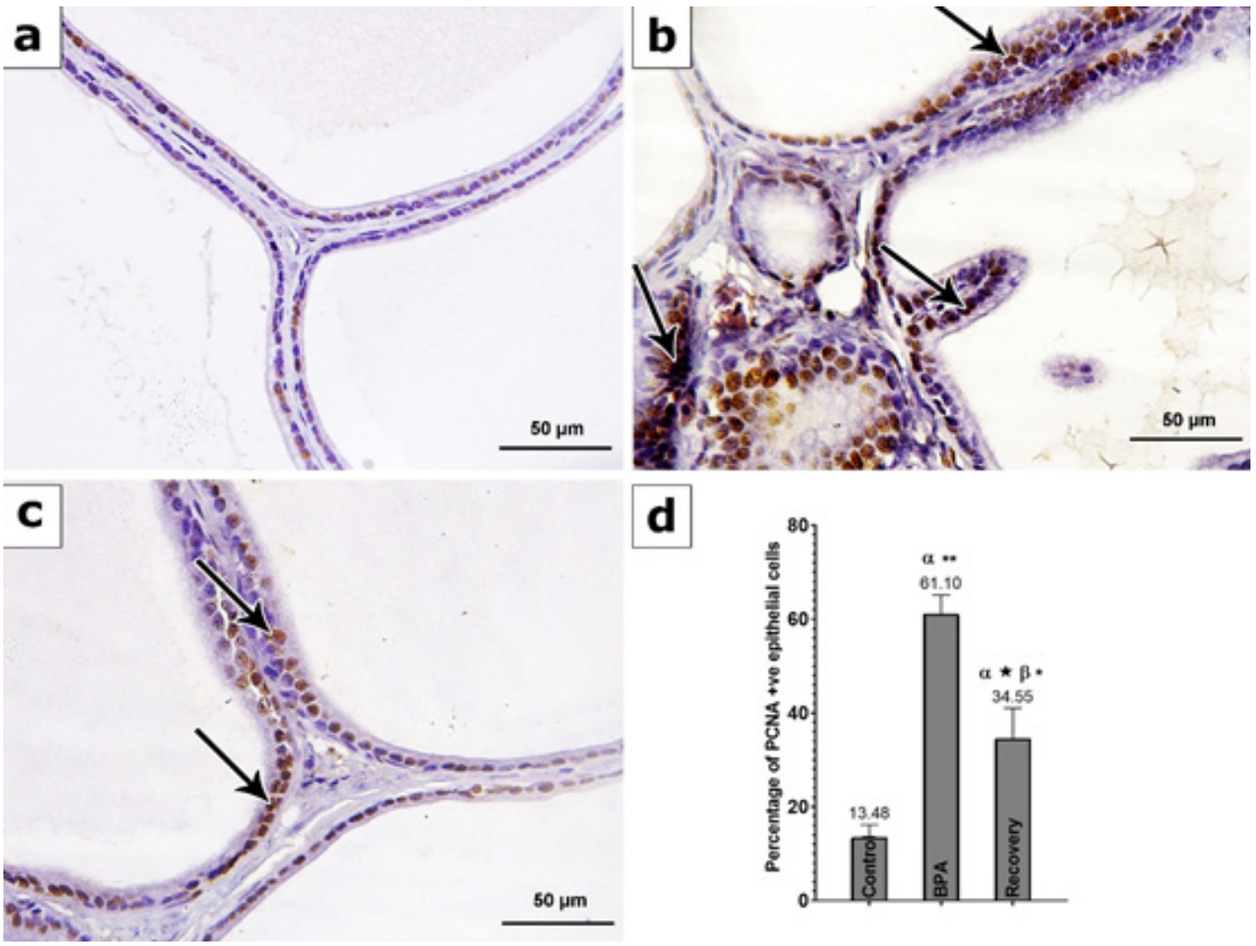

Fig. 6: Photomicrographs showing the estimation of PCNA immunostaining of rat's prostate gland in the three studied groups. (a) Prostate of control rats, (b) Prostate of BA treated rats (c) Prostate of recovery rats. Arrows refer to the dark brown staining of the nuclei of PCNA positive cells. (Anti-PCNA, X400. Scale bar=50 µm). (d) Bar chart showing the quantitative analysis of the PCNA positive cells in the prostate sections of the three studied groups. ** significant at level $p < 0.0001$, * significant at level $p = 0.0058$, * significant at level $p = 0.0251$. α versus control. β versus BPA**.**

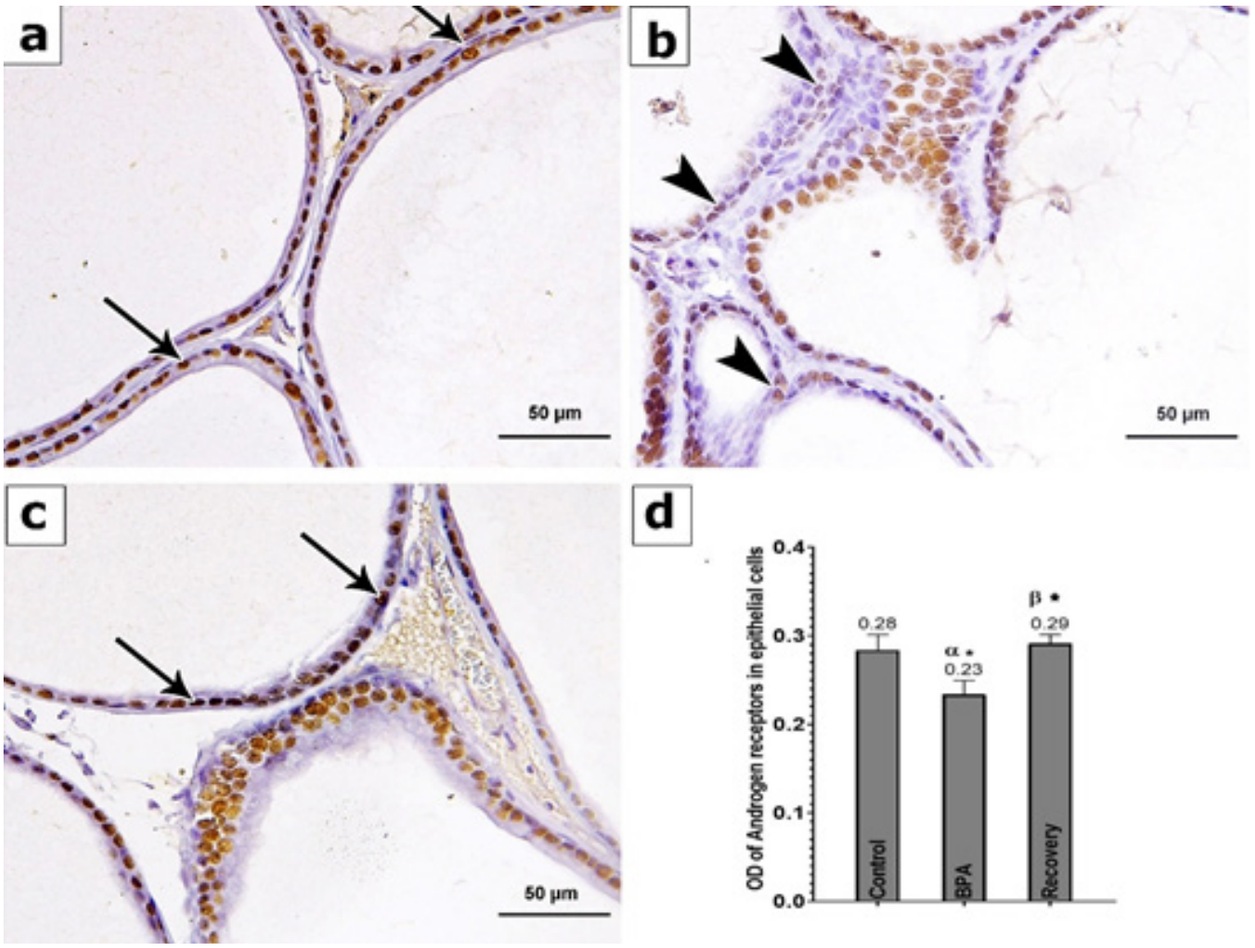

Fig. 7: Photomicrographs showing the expression of AR in the epithelial lining of adult rat's prostate gland from the three studied groups. (a) Prostate of control rats, (b) Prostate of BPA treated rats (c) Prostate of recovery rats. Week expression (arrowhead) in BPA group as compared to the strong expression (arrow) in the control and recovery groups. (Anti-AR, X400. Scale bar=50 µm). (d). Bar chart reveals the optical density of immunocytochemical reaction in experimental groups * significant at level $p = 0.018$, significant at level $p = 0.931$. α versus control. β versus BPA.

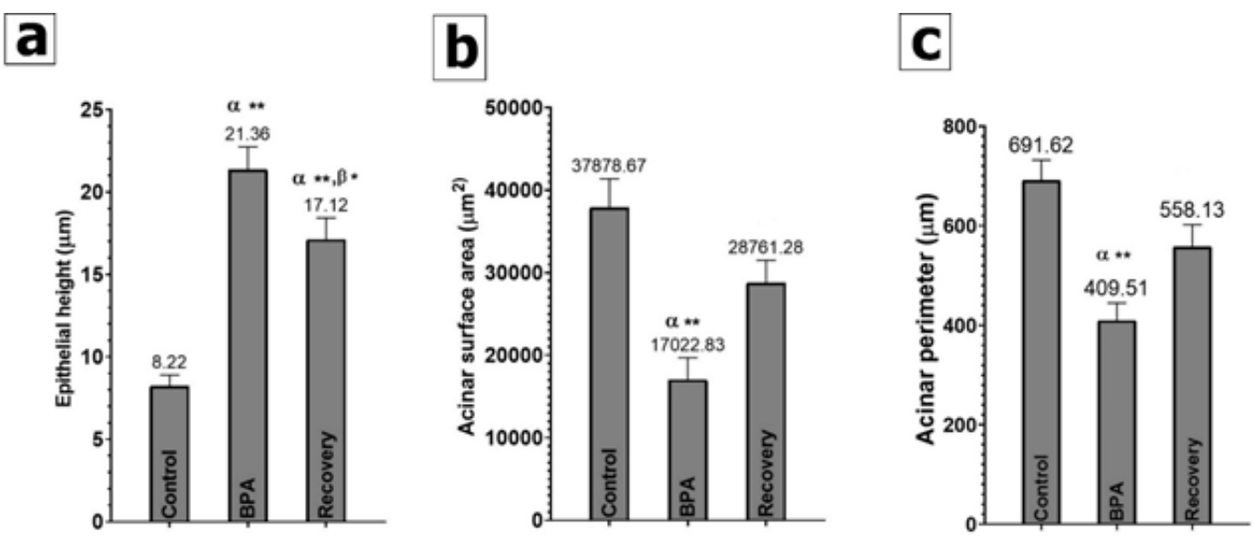

Fig. 8: Bar charts from the three studied groups represent (a): The epithelial height in µm, (b): The acinar surface area in µm2, (c) The acinar perimeter in µm. ** significant at level $p < 0.0001$, * significant at level $p = 0.034$. α versus control. β versus BPA.

DISCUSSION

Due to its ability to disrupt the endocrinological functions, bisphenol A has drawn attention across the globe in the past few years. The hazardous effect of BPA on body systems and particularly male reproductive organs has been established in animal and human studies[24, 25].

The safe exposure to BPA has been determined by the American Environmental Protection Agency by 50 µg/kg/day and more recently by 4 µg/kg/day by the European Food Safety Authority[5]. Nevertheless, a reference dose of 50 mg/kg/day was also experimented, which is the accepted lowest observed adverse effect level (LOAEL)[26].

Although the prostate gland in mouse and rat differs in some anatomical features than in humans, the mouse remains the commonest animal model to study the pathological conditions of the prostate gland[8].

Several common maladies target the prostate gland. Spermatozoa functioning can be disturbed by unhealthy prostate. Homeostasis of the epithelial lining of the prostate gland depends on the cellular influx of zinc and citrate facilitated by androgens[9]. Strong evidence from increasing number of studies indicates that the toxic effect of BPA can changes the morphological structure of prostate[2].

Bisphenol A can disrupt the hypothalamic-pituitary-gonadal axis impairing the gonadotrophins secretion and reduction of serum LH which finally ends in lowering testosterone levels in the blood[27]. In agreement with Castro *et al*.[28] and Zang *et al*.[29], the biochemical analysis of this study showed a significant reduction in testosterone level in the BPA group. In men, increased serum BPA concentration significantly decreased the levels of androstenedione and free testosterone levels, reduced free androgen index and increased sex hormone-binding globulin levels[30]. While BPA inhibited testosterone release in male adolescents, it elevated total testosterone level in the females of the same age group[27].

Regarding the effect of BPA on the structure of the prostatic tissue, the prostatic acini in the BPA group appeared irregular in shape with a reduced lumen that contained scanty faint secretions. The reduction in acinar cavity was confirmed by a significant decrease in perimeter and the surface area in comparison with the control group. Also, the stromal connective tissue between the acini was markedly increased with severely congested blood vessels. Congestion of prostatic vasculature and a significant reduction of the acinar diameter were observed in rats after administration of 10 mg/kg of BPA for 14 days[20]. Olukole *et al*.[31] suggested that diminished lumen of the acinus can reflect its inability to produce secretions. In contrast, Huang *et al*.[32] found slight enlargement of the glandular cavity in the dorsolateral prostate (DLP) of rats treated with 10, 30, and 90µg/kg of BPA /day.

Morphometry of prostatic slides stained with Masson's trichrome in the present study showed a significant increase in the mean area % of collagen fibers in the BPA group compared to the control one. Supporting findings have been reported in previous publications. In utero exposure to 25mg/kg of BPA resulted in a heavy deposition of collagen fibers in the prostate of rats at 21 and 180 postnatal days[33]. In addition, the prostate of adult rats injected with 10 mg/kg BPA intraperitoneally showed deposition of thick collagen bundles around prostatic acini[31].

Recently, the number of elderly males is increasing. Thus, the incidence of benign prostatic hyperplasia (BPH) has been gradually trending upward. In aged rats, a low dose of BPA similar to environmental exposure might change the estrogen/androgen balance that stimulates the proliferation of DLP associated with epithelial-mesenchymal transition[32]. In the present work, there was prominent hyperplasia of the glandular epithelium along with significant increase in epithelial height in the BPA-treated group. According to Wu *et al*.[34], the hyperplasia in the ventral lobe induced by administration of BPA was mediated by upregulation of the androgen-dependent lipocalin-type prostaglandin D synthase (L-PGDS) expression. Meanwhile, the activation of COX-2/NF-κB pathway played a role in hyperplasia induced by the same dosage in the dorsolateral lobe.

Elevated immunolocalization of Proliferating Cell Nuclear Antigen (PCNA) reflects a high rate of cellular proliferation. PCNA is a nuclear protein that is synthesized in the late G1 and early S phases. Therefore, it is considered an accurate indicator of DNA synthesis and cell proliferation[35] Immunohistochemical analysis of this study revealed that the proliferation of acinar epithelium was promoted in the BPA group as shown by a significant increase in the percentage of PCNA positive cells than in vehicle-treated one. This is in concordance with the results of Huang *et al*.,[32] and Wu *et al*.,[34]. Moreover, exposure of neonatal male mice to BPA increased the PCNA immunostaining of spermatogenic cells in the seminiferous tubules[36].

Since the chemical structure of BPA is like naturally occurring estrogens, bisphenol A acts as an estrogen receptor (ER) agonist stimulating endocrinal estrogenic effects[37]. On the other hand, data on the antiandrogenic effect of BPA is controversial[27]. Bisphenol A and its analogues such as bisphenol AF (BPAF) inhibit the functions of androgen receptors (AR) via competition with androgen to bind to AR, thereby down-regulates androgen-induced gene translocation[38, 39].

In the present study, the OD of AR expression in the prostatic epithelium was significantly lower in the BPA group than its value in the control one. In the study of Huang *et al*.[12], BPA decreased the expression of AR in the cultured epithelial cells of ventral prostate. In addition, it has been suggested that the inability of BPA to activate AR was due to its failure to induce functional nuclear foci[38]. Similarly, under the effect of BPA, low spermatogenic activity was associated with diminished expression of AR in the seminiferous tubules of adult rats[40]. Contrasting results were reported in the DLP of BPA-treated rats by Huang *et al*.[32] who clarified that BPA affects the prostatic lobes selectively and dose-dependently.

In the current study, the deleterious changes in the prostate gland that took place under the effect of BPA were incompletely reversed after cessation of BPA administration for 4 weeks. The thickening and hyperplasia of the glandular epithelium was less marked besides, the abundance of the non-glandular tissue and the congestion of blood vessels were less prominent. Also, epithelial height, deposition of collagen, and PCNA score all significantly decreased. Nevertheless, they were still statistically higher than in control. Notably, the expression of androgen receptors, the acinar surface area, and the acinar perimeter were not significantly different than t in the control group. In another study that used the same dosage as in the present study, partial recovery has been observed in histological and biochemical changes of the testicles[41]. However, in the study of Cao *et al*.[14], BPA-induced testicular alterations were reversible only with low doses of BPA (0.05 and 5 mg/kg) and not with 50 mg/kg suggesting that high dose of BPA produces irreversible damage. Since it is lipid-soluble compound, BPA can accumulate in adipose tissue ten folds than its level in the liver. Moreover, its metabolism can be affected by age, gender, and hepatic conditions[42]

CONCLUSION

BPA administration resulted in marked hyperplasia of the prostatic epithelium; significantly increased PCNA score and the laydown of collagen increasing the thickness of the stroma; decreased the OD of AR and the acinar perimeter and surface area significantly. These impacts recovered partially after the stoppage of exposure to BPA.

RECOMMENDATIONS

Further research with prolonged recovery period is needed to confirm or dispute the complete recovery from

BPA effects.

CONFLICT OF INTEREST

There are no conflicts of interest.

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الملخص العربى

الآثار الضارة للبيسفينول أ على البروستاتا عند ذكر الجرذ ألابيض البالغ والدور المحتمل للتعافي: دراسة نسيجية وكيميائية مناعية.

الخلفية:: يتم تصنيع كميات ضخمة من البيسفينول أ في جميع أنحاء العالم. البروستاتا هي الغدة الجنسية الملحقة الرئيسية للذكور من الثدييات. يمكن أن يكون البيسفينول أ سامًا لأنسجة البروستاتا.

الهدف من البحث: التحقيق في تأثير البيسفينول أ على غدة البروستات لدى ذكور الجرذان البيضاء البالغة وإمكانية التعافى.

المواد والطرق: تم تقسيم ثلاثين من ذكور الجرذان البيضاء البالغة (١٨٠-٢٢٠ جم) إلى ثلاث مجموعات. المجموعة الضابطة: حصلت على ١ مل من زيت الذرة بالتزقيم مرة واحدة يوميًا لمدة ثمانية أسابيع. مجموعة البيسفينول أ: اعطيت ٥٠ مليجرام من ثنائى الفينول أ فى ١ مل من زيت الذرة عن طريق الفم يوميا لمدة ثمانية اسابيع. مجموعة التعافى: تعطى البيسفينول أ كما فى المجموعة السابقة ثم تبقى بدون علاج لمدة اربع اسابيع اخرى. في نهاية الدراسة ، تم جمع الدم لقياس هرمون التستوستيرون . تمت إزالة غدة البروستاتا وتجهيزها للتحليل النسيجي والكيميائي المناعي.

النتائج: فى مجموعة البيسفينول أ، انخفض مستوى هرمون التستوستيرون بشكل ملحوظ. شوهد عدم انتظام فى عُنَيبات البروستاتا مع سماكة و تضخم فى ظهارة البروستاتا ووفرة فى السدى مع احتقان الاوعية الدموية فى المقاطع المصبوعه بالهيماتوكسيلين والايوسين. أظهر قياس الشكل أن ارتفاع الظهارة ، وعدد الخلايا الموجبة للمستضد النووي ، ونسبة مساحة الكولاجين كانت أعلى بشكل ملحوظ بينما كانت مساحة سطح ومحيط العُنَيبات والكثافة البصرية لمستقبلات الأندروجين في الخلايا الظهارية أقل بكثير. تم التحلل من هذه التغييرات جزئيًا بعد التوقف عن العلاج بثنائى الفينول أ.

الخلاصة: يمكن أن تتعافى غدة البروستات لدى الجرذان البالغة جزئيًا من الآثار الضارة للبيسفينول أ.