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Investigation of the toxicity effects of bisphenol A (BPA) on the renal function and blood parameter of the laboratory rate

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***Abstract*---**This study was conducted at the College of Science, University of Al-Qadisiyah, to study the relationship between the toxic environmental effects of BPA compound and some biochemical components on the blood of female and male rats, in this study, 60 male and female rats were used, They ranged in age from 8 to 12 weeks, and their weights ranged from 145-200 grams for females and 85-150 grams for males. Rats were divided into four groups according to the dose, with males and females separated. Two control groups: these two groups, three females and three males, dosed 5.0 ml/kg body weight of corn oil per day, group A. Nine females and nine males were fed BPA orally (every day after dissolving in corn oil at 50 mg./kg body weight). Group III (B): 9 females and 9 males were given BPA orally (every day with corn oil, 100 mg/kg body weight). In group C, nine females and nine males were orally injected with a dose of 200 mg/kg BPA dissolved in corn oil every day. The experiment lasted three months. After the end of the first month of animal adaptation, animals were dosed orally for 2 weeks daily. After the first test, the experiment continued for another eight weeks. At the end of that time, the mice were killed and blood and organ samples were taken for the last test, Renal function tests showed a significant increase ($P<0.05$) in serum (urea, creatinine, and uric acid) levels and a decrease in protein in female and male rats treated with 200, 100, and 50, The results of this study found a significant increase ($P<0.05$) in BPA levels in the kidney tissues of male and female rats when given 200, 100, or 50 mg/g BPA for 8 weeks. This study found a significant increase ($P<0.05$) in BPA in kidney tissues of male and female rats after treatment with 200 mg/g. The results of this study showed, as shown in the same table, a significant increase ($P<0.05$) in the concentration of BPA accumulated in the serum of both male and female rats in the groups that took doses of 200 and 100, while the results of this study

showed that the group that took doses of 50 mg / g of BPA did not have such a large increase(P<0.05), RBCs, Hb, PCV percent, and neutrophil percent levels decreased(P<0.05) The 50 mg/g concentration group decreased in male and female rats administered 200 or 100 BPA for two weeks. The results of the trial after 8 weeks showed a substantial drop (P>0.05). in RBCs, Hb, PCV percent, and neutrophil percent in the blood. Study findings Male and female rats administered 200, 100, and 50 mg/g BPA for two weeks exhibited a significant increase(P>0.05). in WBCs, Mono percent, and Eosi percent in their blood. This study likewise demonstrated a significant rise(P>0.05). in WBCs, Mono percent, and Eosi percent in the blood of male and female rats. In the second test, done 8 weeks following the first, the groups were given 200, 100, and 50 mg/g BPA, after comparing them to a corn oil-only control group.

***Keywords*---**investigation toxicity effects, bisphenol A (BPA), renal function, blood parameter, laboratory rate.

Introduction

BPA (2,2-di(p-hydroxyphenyl) propane, BPA) is one of the most widely used industrially manufactured chemicals in the world [1]. Its molecule is small (228 Da), its color is white, and at room temperature, it exists as a solid particle and has an odor of phenol[2]. Bisphenol A (BPA) is a key monomer in plastics and epoxy resins and is utilized as an additive material on both of these materials at the present time. These items gain rigidity, clarity, lightweight, and temperature resistance when BPA is added to the formula. Polycarbonates are utilized in the production of a variety of plastic containers that are utilized often in the food business as well as in residences, including plastic bottles, lenses, and medical equipment. Epoxy resins that contain BPA are frequently used to cover food and beverage cans. Nevertheless, because of the possibility of adverse effects on health[3][4]

The ingestion of foods or beverages that contain the chemical bisphenol-A (BPA) is the most common way that people are exposed to it. Other potential risks include taking in dust particles through the lungs and being exposed to the atmosphere. After the substance has been taken in by mouth, it is absorbed in the gastrointestinal system and then goes through hepatic metabolism, which includes oxidation and hydrolysis. This results in the creation of various metabolites, some of which include BPA monosulfate, BPA glucuronide, and BPA disulfate. Utilizing a combination of techniques, such as solid-phase extraction coupled with isotope dilution, high-performance liquid chromatography, and mass spectrometry, it is possible to determine whether or not BPA and its metabolites are present in bodily fluids such as urine and serum. These bodily fluids include serum and urine.[5]

Bisphenol-A is targeted at multiple organs such as kidneys, liver, spleen, pancreas and lungs [6]100g/kg/day dose of BPA can cause dilation and propagation of glomeruli and degeneration of epithelium of proximal tubule in

kidney. [7] However, to our knowledge there is few researches have done about BPA in Bangladesh. Asian [8] , The current study was planned to estimate the adverse toxic effects of exposure to BPA in male and female albino rats by studying the following parameters BPA toxicity on some blood parameters (RBCs, Hb, PCV percent, neutrophil, WBCs, Mono percent, and Eosi), Study of the Effect of BPA toxicity on Kidney Functions (Urea, Creatinine, Uric acid, and Protein level), Use of high-performance liquid chromatography (HPLC) technology to assess the bioaccumulation of BPA in tissues of the liver, kidneys and brain, as well as in the blood

Material and Methods

Animals

The current study involved 60 rats. 30 adult female rats, and 30 adult male rats of the type Albino rats, obtained from the animal house of the College of Science and College of Veterinary Medicine, University of Al-Qadisiyah, Iraq. Rats' ages ranged from 75 Days, weights ranged from 145–200 g for females and 85–150 g for males. The rats were housed in metal cages to avoid exposure to BPA, which rodents might be subjected to in the case of plastic cages. The cages were fitted with glass bottles to provide the animals with water. The animals were placed in the animal house for 30 days prior to the start of the experiment. This was with the aim of naturalization and adaptation to the atmosphere of the animal house and they were subjected to the light system. 12\12 hours of light and darkness and a temperature of (20-25 C) (20-25 C) The animals were raised in the animal house belonging to the College of Science at the University of Al-Qadisiyah.

Design of the experiment

In this experiment, rats were introduced to the animal house at the Faculty of Science at the University of Al-Qadisiyah. The rats were divided into eight groups after separating the males from the females, according to the figure.

1. control groups: They were divided into two groups: 3 female rats and 3 male rats, which were classified as control groups, were given corn oil only at a concentration of 5.0 ml/kg of body weight every day.
2. Groups (A): were split into two groups: 9 female rats and 9 male rats were given BPA orally (every day after dissolving it in corn oil at a dose of 50 mg/kg of body weight).
3. groups (B): they were divided into two groups, 9 female rats and 9 male rats were given BPA orally (every day after dissolving it in corn oil at a dose of 100 mg/kg of body weight).
4. Groups (C): they were divided into two groups, 9 female rats and 9 male rats, who were dosed with bisphenol-A orally (every day after dissolving it in corn oil at a dose of 200 mg/kg of body weight).

The experiment began on (1/1/2022) and will end on (1/4/2022), The first month was devoted to the rat's adaptation to the new environment, the first rats were dosed orally on BPA daily for six weeks, after which blood samples were collected from the rats for the purpose of the latter test, as shown in Figures.

BPA compound

The trade name for the chemical is BPA (97.0 percent, CAS 80-05-7), and it was obtained from the Indian CDH Company. Pure corn oil was used in the dissolution of the BPA compound as well as in the dosing of the control group, A BPA solution was generated by dissolving BPA in maize oil on a weekly basis, and each group received a dose of this solution based on their body weight, with the control group receiving simply corn oil.

Sampling Blood Collection

Rats were weighed and anesthetized by placing them in a cotton bag filled with anesthetic chloroform, then closed with a rubber band, and blood samples were taken by heart stab method. Blood samples were collected for primary tests. Samples were also collected eight weeks after BPA ingestion of phase II doses for final tests.

Then half of the blood samples were placed in a sterile, dry tube, an anticoagulant container for blood tests, and the other half of the samples were placed in a tube that did not contain an anticoagulant, and then placed in a centrifuge (3000 cycles/min) for 15 minutes for the purpose of obtaining blood serum for the purpose of conducting blood and biochemical tests. The necessary tests were conducted directly, as the collection of blood samples was in two stages: two weeks for the first test, and the collection of other samples in six weeks after the initial test.

Estimation of Kidney function standards

Determination of Serum Uric acid [9]

Principle: This assay depends on the oxidation of Uric acid by Uricase to Allantoine and Hydrogen peroxide according to the following reaction:

$$\text{Uric acid} + O2 + 2H2O \xrightarrow{\text{Uricase}} \text{Allantoine} + CO2 + H2O2$$

$$2H2O2 + \text{DHBS} + 4-\text{aminoantipyrine} \rightarrow \text{Red quinone} + H2O + HCl \text{ (in presence of peroxidase).}$$

Determination of Serum Total protein [10]

Principle: The principle of this method, the proteins give an intensive violet-blue complex with copper salts in an alkaline medium. Iodide is included as an antioxidant. The intensity of the color formed is proportional to the total protein concentration in the sample. The absorbance of the sample against blank was read at the wavelength 540 nm.

Determination of Serum Urea Level[11]

A: Principle: This method is based on the fact that Urea is hydrolyzed by water and Urease into ammonia and Carbon dioxide. The ammonia produced is further acted with hypochlorite and salicylate to form a green complex.

$$Urea + H2O \rightarrow 2NH3 + CO2$$

The absorbance was done at 600 nm.

Determination of Serum Creatinine Concentration[12]

principle: It is based on the idea that Creatinine in alkaline picrate solution, forms a color complex. The rate of formation of the complex is measured at 500 nm.

HPLC Analysis

Animal sacrifice and organ collection

Prior to sacrifice, rats were weighed and anesthetized by placing them in a cotton-lid container tray filled with anesthetic chloroform, which was then closed with a rubber band, To access the organs used in the study, the abdominal cavity was opened by cutting the midline in the abdomen to make an opening. The kidneys, liver, and brain were taken from the animal cavity and stored at a high degree of freezing until the required tests could be performed on the organs using high-resolution liquid chromatography (HPLC).

Sample preparation

1- tissue (170 mg) homogenized by tissue homogenizer
2- serum samples (500ul) or the homogenized tissue were mixed with 3 ml of hexane and shacked for 3 min
3- five ml of acetonitrile was added and shacked for 3 min
4- the mixture was centrifuged at 2500 rpm FOR 15 MIN
5- the acetonitrile layer (lower layer) was transferred and filtered by a syringe filter (0.2um)
6- the filtrate was concentrated under vacuum to 500 ul and injected to HPLC system The High-Performance Liquid Chromatography (HPLC) system used in this study was an HPLC, The components of this system are according to the table below:

Table (1) The components of HPLC system

	Component	Model or version	Company and origion
1	Binary high-pressure gradient pump	P6.1L	Knuaer, Germany
2	Diode array detector	DAD 2.1L	Knuaer, Germany
3	Sample loop (20 µl) and injector	D1357	Knuaer, Germany

4	Analyses and system control software	Claritychrom, V 7.4.2.107	Dataapex, Czech Republic

The High-Performance Liquid Chromatography (HPLC) system used in this study was an HPLC Waters 2690 with an autosampler system and UV detector set to 210 nm. A 250 x 4.6 mm Sum Waters C18 Column was used to prepare the sample. Ten microliters of samples were put into the chromatographic system for analysis in isocratic clution at 1 ml/min at room temperature with a mobile phase of water/acetonitrile (40:60, v/v) for 17 minutes.

When comparing the retention time and absorption spectra of each chemical to the standards, the detection of each compound was accomplished. The concentration was determined by using repeated concentrations of the external standard substances in order to construct a calibration curve between the concentration and the equivalent peak area of the external standard substances[13].

Results

Toxic Effect of BPA on kidney function

The results of the current study showed that there was an increase in the significant differences at ($P < 0.05$) in Levels of urea in serum in all treatment groups compared to the control group, Between group A and group C and between group B and group C, the results of the current study showed that there was an increase in significant differences at ($P < 0.05$) in Levels of urea in serum in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was an increase in the significant differences at ($P < 0.05$) in Levels of urea in serum in all treatment groups compared to the control group, where the results of our study showed that there was a significant increase at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing. Table 3-1

The results of the current study showed that there was an increase in the significant differences at ($P < 0.05$) in levels of creatinine in the serum in all treatment groups compared to the control group, Between group A and group C and between group B and group C, the results of the current study showed that there was an increase in significant differences at ($P < 0.05$) in levels of creatinine in the serum in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was an increase in the significant differences at ($P < 0.05$) in levels of creatinine in the serum in all treatment groups compared to the control group, where the results of our study showed that there was a significant increase at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing. Table 3-1

The results of the current study showed that there was an increase in the significant differences at (P < 0.05) in uric acid concentration in all treatment groups compared to the control group, Between group A and group C and between group B and group C, the results of the current study showed that there was an increase in significant differences at (P < 0.05) in uric acid concentration in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was an increase in the significant differences at (P < 0.05) in uric acid concentration in all treatment groups compared to the control group, where the results of our study showed that there was a significant increase at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing. Table 3-1

The results of the current study showed that there was a decrease in significant differences at (P < 0.05) in the total amount of protein in all treatment groups compared to the control group, Between group A and group C and between group B and group C, and the results of the current study showed that there was a decrease in significant differences at (P < 0.05) in the total amount of protein in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was a decrease in significant differences at (P < 0.05) in the total amount of protein in all treatment groups compared to the control group, where the results of our study showed that there was a significant decrease at the second test in eight weeks of dosing compared to the first test In the two weeks of dosed. Table 3-1

MALE						
Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
2 WEEKS	Urea	22.01±2.11 D	36.51±2.63 A	31.05±3.05 B	26.99±1.98 C	3.01
	Creatinine	0.621±0.02 D	1.852±0.12 A	1.231±0.23 B	1.052±0.21 C	0.51
	Uric acid	1.65±0.24 D	3.54±0.36 A	2.66±0.51 B	2.11±0.33 C	0.88
	Total protein	2.21±0.26 A	0.93±0.04 D	1.35±0.22 C	1.74±0.24 B	0.56
FEMALE						
Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
2 WEEKS	Urea	21.05±2.31 D	38.54±2.96 A	32.14±3.00 B	27.44±1.65 C	1.55
	Creatinine	0.651±0.01 D	1.874±0.27 A	1.412±0.35 B	1.022±0.21 C	0.41
	Uric acid	1.67±0.33 D	3.15±0.95 A	2.14±0.36 B	1.95±0.41 C	0.46

	Total protein	2.32±0.89 A	1.05±0.26 D	1.41±0.55 C	1.86±0.63 B	0.13
MALE						
Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
6 WEEKS	Urea	22.01±2.11 D	46.21±3.52 A	39.63±3.66 B	28.63±3.01 C	2.11
	Creatinine	0.622±0.02 D	2.112±0.55 A	1.532±0.63 B	1.105±0.45 C	0.42
	Uric acid	1.65±0.55 D	4.96±0.95 A	3.56±0.64 B	2.84±0.58 C	0.74
	Total protein	2.23±0.65 A	0.75±0.01 D	1.01±0.21 C	1.52±0.29 B	0.45
FEMALE						
Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
6 WEEKS	Urea	21.05±2.01 D	48.52±3.22 A	41.20±3.28 B	29.33±2.96 C	1.06
	Creatinine	0.651±0.01 D	2.051±0.53 A	1.201±0.61 C	29.33±2.96 C	0.36
	Uric acid	1.67±0.21 D	4.21±0.96 A	3.11±0.88 B	2.41±0.53 C	0.41
	Total protein	2.32±0.51 A	0.62±0.03 D	1.01±0.22 C	1.42±0.26 B	0.22

Table 3-1 Toxic effect of different doses of BPA on kidney function

The results of the current study showed a completely negative correlation at (-1.0) in kidney Function During the exposure period BPA for male and female rats ranging from 2 to 8 weeks, where the results of the current study showed that there is a completely negative correlation at (-1.0) in Urea During the exposure period of BPA for males and female rats that ranged from 2 to 8 weeks. Table (3-2)

the results of the current study showed that there is a completely negative correlation at (-1.0) in Creat. During the exposure period of BPA for males and females, rats ranged from 2 to 8 weeks. Table (3-2)

also, the results of the current study showed that there is a completely negative correlation at (-1.0) in Uric Acid During the exposure period of BPA for males and female rats that ranged from 2 to 8 weeks. Table (3-2)

the results of the current study showed that there is a completely negative correlation at (-1.0) in the Total Protein During the exposure period of BPA for males and female rats ranged from 2 to 8 weeks. Table (3-2)

Table (3-2) Correlation Coefficient between 2 weeks and 8 weeks of Dosing BPA on kidney Function

Correlation Coefficient	Males			
	Urea	Creat.	Uric acid	Total

				protein
	0.9879	0.9889	0.9920	0.9494
	Females			
	Urea	Creat.	Uric acid	Total protein
	0.98919	0.9939	0.9627	0.9833

Effect of BPA on the Blood Parameter

The results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in RBCs levels in all treatment groups compared to the control group, Between group A and group C and between group B and group C, and the results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in RBCs levels in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in RBCs levels in all treatment groups compared to the control group, where the results of our study showed that there was a significant decrease at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing Table (3-3)

The results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in Hb levels in all treatment groups compared to the control group, Between group A and group C and between group B and group C, and the results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in Hb levels in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in Hb levels in all treatment groups compared to the control group, where the results of our study showed that there was a significant decrease at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing Table (3-3) Table (3-4)

The results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in PCV%, neutrophil% levels in all treatment groups compared to the control group, Between group A and group C and between group B and group C, and the results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in PCV%, neutrophil% levels in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was a decrease in significant differences at ($P < 0.05$) in PCV%, neutrophil% levels in all treatment groups compared to the control group, where the results of our study showed that there was a significant decrease at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing Table (3-3) Table (3-4)

The results of the current study showed that there was an increase in the significant differences at (P < 0.05) in WBCs levels in all treatment groups compared to the control group, Between group A and group C and between group B and group C, the results of the current study showed that there was an increase in significant differences at (P < 0.05) in WBCs in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was an increase in the significant differences at (P < 0.05) in WBCs levels in all treatment groups compared to the control group, where the results of our study showed that there was a significant increase at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing. Table (3-3) Table (3-4)

The results of the current study showed that there was an increase in the significant differences at (P < 0.05) in Mono%, and Eosi% levels in all treatment groups compared to the control group, Between group A and group C and between group B and group C, the results of the current study showed that there was an increase in significant differences at (P < 0.05) in Mono%, and Eosi% in all treatment groups compared to the control group, where the results of our study showed that there is a significant increase between groups of females compared to With the male groups, the results of the current study showed that there was an increase in the significant differences at (P < 0.05) in Mono%, and Eosi% levels in all treatment groups compared to the control group, where the results of our study showed that there was a significant increase at the second test in eight weeks of dosing compared to the first test In the two weeks of dosing. Table (3-3) Table (3-4)

Table (3-3) Effect of BPA on Blood Parameter for 2 weeks

MALE						
Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
2 WEEKS	RBCs	6.55±0.52 A	2.11±0.21 D	3.54±0.36 C	4.85±0.39 B	1.01
	Hb	13.11±0.63 A	6.52±0.55 D	8.63±0.65 C	10.22±0.87 B	1.63
	PCV%	41.21±2.14 A	22.01±1.62 D	29.63±1.02 C	38.52±1.56 B	5.21
	WBCs	8.25±0.53 D	18.54±0.98 A	14.22±0.77 B	11.05±0.99 C	2.11
	Lymph. %	65.52±11.21 C	85.21±10.32 A	72.54±9.52 B	66.52±8.96 C	8.05
	Neutr. %	22.42±2.11 A	14.21±1.02 D	16.52±1.21 C	19.53±1.33 B	2.54
	Mono. %	6.21±0.56 C	9.55±0.85 A	7.58±0.69 B	6.57±0.58 C	1.05
	Eosi. %	3.45±0.25 D	6.62±0.63 A	5.21±0.41 B	4.31±0.33 C	0.52
FEMALE						

Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
2 WEEKS	RBCs	6.58±0.56 A	2.51±0.25 D	3.66±0.37 C	4.96±0.41 B	1.25
	Hb	13.05±0.66 A	7.52±0.58 D	9.21±0.69 C	11.02±0.94 B	1.86
	PCV%	40.22±2.05 A	25.21±1.51 D	33.54±1.12 C	38.21±1.63 B	3.55
	WBCs	8.35±0.85 D	15.94±0.96 A	11.42±0.87 B	9.15±0.95 C	1.01
	Lymph. %	65.52±12.11 D	89.11±10.66 A	70.34±9.85 B	67.12±8.63 C	2.52
	Neutr. %	22.42±2.10 A	15.31±2.00 D	17.62±1.85 C	20.03±1.64 B	1.41
	Mono. %	6.21±0.51 D	10.15±0.98 A	8.64±0.66 B	7.68±0.74 C	1.06
	Eosi. %	3.45±0.26 D	7.63±0.66 A	5.88±0.58 B	4.22±0.49 C	1.00

Table (3-4) Effect of BPA on Blood Parameter for 8 weeks

MALE						
Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
6 WEEKS	RBCs	6.55±0.51 A	2.52±0.25 D	3.95±0.33 C	5.59±0.46 B	0.95
	Hb	13.11±0.85 A	4.53±0.56 D	6.58±0.66 C	9.14±0.78 B	2.01
	PCV%	41.21±2.01 A	20.01±1.02 D	31.13±1.56 C	36.32±1.77 B	5.01
	WBCs	8.25±0.85 D	20.04±1.52 A	16.32±1.06 B	13.25±0.98 C	2.01
	Lymph. %	65.52±11.02 D	88.32±10.54 A	79.54±9.85 B	69.99±8.54 C	3.56
	Neutr. %	22.42±2.14 A	15.31±1.96 D	17.62±1.45 C	20.93±1.66 B	1.85
	Mono. %	6.21±0.56 D	10.21±0.86 A	8.36±0.77 B	7.62±0.68 C	0.95
	Eosi. %	3.45±0.22 D	7.02±0.36 A	5.66±0.29 B	4.35±0.45 C	0.85
FEMALE						
Period	Parameter Mg\dl	Control	A (200 mg\kg)	B (100 mg\kg)	C (50 mg\kg)	LSD
6 WEEKS	RBCs	6.58±0.52 A	3.59±0.33 D	4.67±0.69 C	6.98±0.84 B	1.86
	Hb	13.05±0.95 A	6.21±0.61 D	8.21±0.66 C	10.11±0.93 B	1.74
	PCV%	40.22±2.00 A	29.28±1.03 D	34.74±1.54 C	39.01±1.63 B	1.01

	WBCs	8.35±0.66 C	16.54±0.99 A	10.32±0.96 B	7.42±0.89 D	1.05
	Lymph. %	65.52±11.25 D	91.22±10.33 A	80.24±9.85 B	79.63±8.47 C	8.21
	Neutr. %	22.42±2.41 A	14.02±1.69 D	16.35±1.45 C	18.96±1.74 B	1.66
	Mono. %	6.21±0.56 D	11.23±0.89 A	9.63±0.73 B	7.52±0.69 C	1.09
	Eosi. %	3.45±0.21 D	9.21±0.69 A	7.33±0.53 B	5.21±0.49 C	0.99

Effect of BPA on some tissues of the body organs

The results of the current study showed an increase in the significant differences at ($P < 0.05$) in the accumulation of BPA in kidney tissue in all treatment groups compared to the other groups, were between group A and group B and between group B and group C, group A and group C, which showed The results of the current study that there is an increase in statistically significant differences at ($P < 0.05$) in the kidney tissue of males and females rats in all treatment groups. The results of our study showed that there is a significant increase among female groups, compared to male groups, table (3-5)(3-6)

The results of the current study showed an increase in the significant differences at ($P < 0.05$) in the accumulation of BPA in serum of blood in all treatment groups compared to the other groups, were between group A and group B and between group B and group C, group A and group C, which showed The results of the current study that there is an increase in statistically significant differences at ($P < 0.05$) in the serum of blood of males and females rats in all treatment groups. The results of our study showed that there is a significant increase among female groups, compared to male groups table (3-5)(3-6)

Table (3-5) Effect of BPA through its accumulation in the tissues of the organs for male

Organs	Groups	BPA	ug/ml	ug/g tissue
Kidney	A	20.9±2.11 A	0.5718±0.32 A	1.68±0.41 A
	B	13.86±1.63 B	0.3796±0.11 A	1.12±0.36 B
	C	6.35±0.95 C	0.1747±0.12 B	0.51±0.05 C
LSD	0.46			
Serum	A	19.41±1.85 A	0.5312±0.25 A	0
	B	13.76±1.66 B	0.3769±0.15 A	0
	C	2.96±0.58 C	0.0821±0.01 B	0
LSD	0.24			

Table (3-6) Effect of BPA through its accumulation in the tissues of the organs for male

Organs	Groups	BISPH.	ug/ml	ug/g tissue
Kidney	A	19.39±2.10 A	0.5306±0.30 A	1.56±0.46 A
	B	13.86±1.69 B	0.3796±0.12 A	1.12±0.33 A
	C	3.64±0.92 C	0.1008±0.15 B	0.30±0.02 B
LSD	0.55			
Serum	A	5.95±1.80 A	0.1638±0.23 A	0
	B	4.68±1.68 B	0.129±0.19 B	0
	C	2.96±0.51 C	0.0821±0.02 C	0
LSD	0.36			

Discussion

The results of this study showed that exposure to BPA increased serum levels of urea, creatine, and uric acid in both male and female BPA-treated rats at all oral doses (200, 100, and 50 mg/kg) within two weeks of starting the experiment. And rats treated with BPA for eight weeks with oral doses (200, 100, and 50 mg/kg) for eight weeks showed a significant increase in serum urea, creatine, and uric acid levels in males and females as compared to the control group.The present results are in agreement with previously published results[14].[15][16] According to the findings of this research, giving rats the highest possible dose of BPA for 15 days led to a considerable increase in the levels of serum urea and creatinine, which was indicative of compromised renal function.The results of this study indicated that exposure to BPA led to a slight decrease in the protein levels of mice treated with BPA at all oral doses (200, 100, and 50 mg/kg) within two weeks. This study showed that exposure to BPA for eight weeks resulted in a significant decrease in protein levels. At all oral doses (200, 100, and 50 mg/kg), the decrease in protein levels was greater in females than the reduction in BPA for eight weeks. The amount of protein present in males.The present results are in agreement with previously published results.[8]. According to the findings of this research, when compared to the controls group, the amount of total serum protein was found to be lower at dosages of 50 and 100 mg/kg, while it was shown to be higher in urine at the dose of 50 mg/kg.The findings of this research indicated that the renal function of female rats was negatively impacted more than that of male rats, regardless of the oral doses tested, and the reason for this was the [17] BPA has a nephrotoxic effect due to accumulation of BPA toxic metabolites and inability of the kidney to eliminate those.This study found a significant increase in the concentration of BPA in the kidney tissues of male and female rats treated with concentrations of 100 and 200 mg/kg and a small percentage in the group treated with a concentration of 50 mg/kg. These results are consistent with previous research. The study (Haroun *et al.,* 2019) found that BPA is bad for the kidneys because it causes toxic BPA products to build up and

the kidneys can't get rid of them.Bisphenol is a molecule with estrogenic and endocrine-disrupting activity. It has a phenolic structure that is excluded by the kidneys, and its concentration increases when it is less filtered by the glomeruli. Phenol is one of the toxins that has been linked to impaired kidney function and damage to blood vessels.[18]. This study revealed a significant increase in the levels of WBCs in female and male rats treated with doses of 200, 100, and 50 mg/kg BPA for 2 weeks. This study showed that female and male rats who were given the same doses of BPA for eight weeks significantly increased the levels of WBCs. The results of this study were consistent with the study[19], which confirmed the presence of a significant increase in the number of white blood cells in females. Rats that were exposed to 250 mg/kg/body weight of BPA were compared to the other treated groups, and this study confirmed that there were increases in WBC value after exposure to 250 mg/kg/body weight of BPA, which may be explained by the role of BPA in the induction of inflammatory conditions or may be due to increased neutrophil count. A higher number of white blood cells can also be caused by BPA-related stress and the immune system being boosted. This study revealed a significant decrease in hemoglobin, PCV and RBC levels in female and male rats treated with doses of 200, 100 and 50 mg/kg BPA for two weeks. This study showed that female and male rats given the same doses for eight weeks of exposure to BPA significantly decrease in hemoglobin, PCV and RBC levels . The results of this study were consistent with the study.([16])This study showed a significant decrease in hemoglobin, PCV and RBC concentrations of BPA-exposed mice by 100 mg compared to the control group. BPA has the potential to hinder the manufacture of hemoglobin or the lysis of RBC. Additionally, BPA has the ability to modify the structure of hemoglobin, which has the potential to impact the physiological activities of hemoglobin[20]. Bisphenol-A produces a considerable decrease in viability, osteogenic differentiation in the bone marrow mesenchymal stem cells, and aberrant development in bone, all of which contribute to generation of insufficient RBC. .[21]

Conclusions

From the results of the current study, it was concluded that Bisphenol A is a harmful substance and causes impairment in kidney function, which leads to an increase in the levels of urea, creatinine and uric acid and causes a decrease in the level of total protein in the kidneys. This accumulates in the kidney tissues and the kidneys cannot get rid of it, causing impairment in kidney function due to its high toxicity. Females were more affected than males when exposed to bisphenol A because of the many disorders that were confirmed in this study in all biochemical indicators

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