JJBS

Jordan Journal of Biological Sciences

Volume 11, Number 4, September 2018
ISSN 1995-6673
Pages 461 - 467

Bisphenol-A Hepatotoxicity and the Protective Role of Sesame Oil in Male Mice

Osama H. Elhamalawy[1], Fawzy I. Eissa[2], Aida I. El Makawy[2,*] and Mahmoud M. EL-Bamby[1]

[1]Department of Environment and Bio-Agriculture, Faculty of Agriculture, Al-Azhar University, Cairo; [2]Department of Cell Biology, National Research Center, 33 El Bohouth Street, Dokki- Giza-Egypt-P.O.12622.

Received January 23, 2017; Revised February 20, 2018; Accepted February 27, 2018

Abstract:

The present study is conducted to estimate the protective effects of sesame oil (SO) against bisphenol-A (BPA) induced hepatotoxicity in male mice. BPA (50 mg/kg b wt) was gavages orally to mice once a day for twenty-eight successive days. While, SO was administered to the mice orally at 1 mL/kg b wt. through three regimens (before, with or after) treatment of BPA. After the complementation of treatments, the liver of each sacrificed animal was subject to DNA damage evaluation using alkaline comet assay and histopathological examination. In addition, blood was collected for biochemical assessment of the liver function. Results showed that, BPA significantly reduced the relative liver weight, and caused DNA damage, several histopathological alterations in liver tissue and elevation in ALT and AST compared to the control. On the contrary, oral gavages of SO with BPA was effective in the increase of relative liver weight, amelioration of DNA damage and histopathological alterations, and in the reduction of the liver enzyme levels compared to BPA's treated mice. Furthermore, the best alleviation of the undesirable effects of BPA appears in the administration of SO to mice before the BPA treatment, followed by after treatment and during or with BPA treatment. In conclusion, the present study provided clear evidence that SO possesses a promising protective activity against the noxious effects of BPA.

Keywords: Bisphenol-A, Hepatotoxicity, Sesame oil, DNA damage, Histopathological alterations.

1. Introduction

Bisphenol-A (BPA) is a famous endocrine disruptor fabricated compound (Michalowicz, 2014) widely utilized in the manufacturing of polycarbonates, epoxy resins and thermal paper (Hoekstra and Simoneau, 2013), food and beverage containers, utensils, baby tools, protective coatings and CD (Maffini *et al.*, 2006; Biedermann *et al.*, 2010).

A huge quantity of BPA is continuously released into the environment through different routes, including sewage, landfill leach and domestic waste combustion (Gassara *et al.*, 2013). Therefore, BPA has become ever-present in the environment (Flint *et al.*, 2012). Healthwise, BPA causes hepatotoxic, mutagenic, reproductive and carcinogenic effects (Doherty *et al.*, 2010; Erler and Novak, 2010; Meeker *et al.*, 2010; Zeinab *et al.*, 2012). Moreover, Lee *et al.* (2003) stated that BPA induced DNA strand-breaks in mouse lymphoma cells. In addition, it can induce liver, kidney, brain, and other organ injuries by generating reactive oxygen species (ROS) (Bindhumol *et al.*, 2003; Kabuto *et al.*, 2004).

Sesame oil (SO) is obtained from the *Sesamum indicum* L. seeds that belong to the family of Pedaliaceae. It contains many fatty acids and antioxidants, including sesamin, sesamolin, sesamol, and tocopherol, (Fukuda, 1990). Furthermore, it offers lipid peroxidation, the best protection by increasing nonenzymatic and enzymatic antioxidants (Sankar *et al.*, 2005). Many studies revealed that SO attenuated the hepatotoxicity induced by numerous compounds in experimental animals (Erol *et al.*, 2011; Srinivasan and Liu, 2012; Periasamy *et al.*, 2012; 2014; Azab, 2014; Soliman *et al.*, 2015). Whereas, Cengiz *et al.* (2013) reported that SO treatment was not significantly effective in the mitigation of histopathological disturbances in CCl_4 treated rat liver. Therefore, the present research is designed to evaluate the protective effects of SO against the hepatotoxicity induced by BPA in male mice.

2. Materials and Methods

2.1. Chemicals

Bisphenol-A (BPA) (≥ 99 %) was purchased from Sigma-Aldrich Company (St. Louis, MO, USA). Commercial sesame oil was purchased from EL Captin

* Corresponding author. e-mail: : eaelmakawy@yahoo.com,vbdig2set@hotmail.com.

Company (Al Obour City, Cairo, Egypt). The aspartate aminotransferase (AST) and alanine aminotransferase (ALT) kits were purchased from Biodiagnostic co., Egypt. All other chemicals were of analytical grade and were purchased from standard commercial suppliers.

2.2. Dose Preparation

BPA was dissolved in absolute ethyl alcohol (95 %) and diluted with corn oil [1:20 alcohol: corn oil (vehicle)] to obtain a final concentration of BPA (50 mg/kg b wt). It was freshly prepared before use.

2.3. Animals and Treatments

Male Swiss albino mice weighing 26±5 g (10-12 week old) were purchased from Theodor Bilharz Research Institute, Giza, Egypt. They were housed in polypropylene cages (43×30×15cm, 5 mice per cage) with stainless steel covers in the Animal House of Environment and Bioagriculture Department, Faculty of Agriculture, Al-Azhar University. The animals were kept under controlled temperature (23±4 °C), 50–55 % relative humidity, and a photoperiod of 12 hours of light: 12 hours of dark cycle. After acclimation for two weeks, the animals were randomly divided into seven groups (n = 10) with approximately equal mean body weights. Animals were administered orally for twenty-eight successive days for BPA (50 mg/kg b wt) and/or SO (1mL/kg b wt) either before, with, or after the BPA administration as follows: group one (control); group two (vehicle); group three (SO); group four (BPA); group five (SO before BPA); group six (SO with BPA) and group seven (SO after BPA).

2.4. Oil Analysis

2.4.1. Fatty Acids Analysis

The fatty acid profile was determined as fatty acid methyl esters by Thermo scientific TRACE 1310 gas chromatograph attached with ISQ LT single quadrupole mass spectrometer (GC-MS). The preparation of the fatty acid methyl esters (FAMEs) was performed according to the procedure of AOAC (2000). A sample of the oils (50 mg) and 1 % H_2SO_4 in absolute methanol were put in screw-cap vial (2 mL). The vial was covered under a stream of nitrogen before being heated in an oven at 90 ^oC. Finally, 1µL of the solution obtained was injected into the GC–MS system after the addition of the internal standard. The fatty acid methyl esters (FAMEs) composition analysis was performed in an Thermo scientific TRACE 1310 gas chromatograph attached with ISQ LT single quadrupole mass spectrometer with DB1, 15m; 0.25mm ID (J&W scientific) capillary column. Helium was used as a carrier gas with a flow rate of 1.5 mL min^{-1}, and the injector temperature was maintained at 200^o C. the oven temperature was programmed with an initial temperature of 115^o C for one minute and was then increased to 280^o C by 7.5^o C min^{-1} for three minutes.

2.4.2. Total Phenolic Content

The total phenolic content (TPC) was determined using the Folin–Ciocalteau's reagent according to the method reported by Lin and Tang (2007) at 760 nm with spectrophotometer (UV-1601; Shimadzu, Tokyo, Japan. The quantification was done on the basis of the standard curve of gallic acid concentration ranging between 10 to 80 mg/mL (r^2= 0.99).

2.4.3. Determination of the Total Tocopherol (Vitamin E)

High performance liquid chromatography (HPLC) system (1100 series, Agilent Technologies) was used for the quantification of vitamin E based on a method described by Gimeno *et al.* (2000). The oil sample was diluted in hexane (1:10). Thereafter, 200 µL was transferred to a screw-capped tube, where 600 ml of methanol and 200 mL of the internal standard solution (300 µg/mL of α-tocopherol acetate in ethanol) were added. After being vortex-mixed and centrifuged (3000 g, 5 min), the samples were filtered through a 0.45 mm pore size filter, and an aliquot of the overlay was directly injected into the chromatograph.

2.4.4. Measurement of the Antioxidant Activity

The ability of SO at 200 uL to scavenge 2.9 mL of 1, 1'-diphenyl 1-2-picrylhydrazyl (DPPH) free radical was estimated by the method of Singh *et al.* (2002).

2.5. Relative Liver Weight

At the termination of the experiments, livers were dissected out, trimmed of excess fat and weighed before the genetic and histopathological studies took place. The liver weight was presented as relative organ weight as follows:

$$\text{Relative organ weight} = \frac{\text{Absolute organ weight (g)}}{\text{Final body weight (g)}} \times 100$$

2.6. Evaluation of DNA Damage

2.6.1. Comet Assay in the Liver Cells

The comet assay was performed in the liver cells according to Bandyopadhyaya *et al.* (2008). Briefly, 50 µL of cell suspension was mixed with 100 µL of 1 % low melting point (LMP) agarose and were added to fully-frosted slides coated with 80 µL of 1 % normal melting point (NMP) agarose. The cells were then incubated in a lysis solution (2.5 mol L^{-1} NaCl, 100 mmol L^{-1} EDTA, 10 mmol L^{-1} Tris-HCL, 1 % Triton X-100, pH 10) at 4 °C for at least two hours, at which the slides were placed into an alkaline solution (300 mmol L^{-1} NaOH, 1 mmol L^{-1} EDTA, pH 13) at 4 °C for twenty minutes to allow for the DNA unwinding, and were electrophoresed at 25 V (300 mA) for twenty minutes . Finally, the slides were neutralized in a 400 mmol L^{-1} Tris buffer (pH 7.5) for fifteen minutes and were stained with ethidium bromide (5 µg mL^{-1}). Images of fifty randomly selected nuclei per experimental group were captured using a fluorescence microscope (Eclipse 800, Nikon, Tokyo, Japan). They were analyzed with image analysis software (Comet Assay IV, Perceptive Instruments, Suffolk, UK). The scored parameters included the tail length, DNA percentage in tail and olive tail moment (OTM). Tail length is the maximum distance that the damaged DNA migrates from the center of the cell nucleus. The percentage of DNA in Tail is the DNA content that migrates from the nucleus into the comet tail. OTM is the product of the tail length and percentage of DNA, which gives a more integrated measurement of the overall DNA damage in the cell.

2.7. Histopathological Examination

Liver from each sacrificed mouse was dissected out and trimmed of excess fat tissues. The tissues were fixed in 10 % buffered formalin and were processed for paraffin sectioning by dehydration in different concentrations of alcohol, cleared with xylol, and embedded in paraffin blocks. Sections of about 5µm thick were stained with Harris haematoxylin and eosin (H&E) for a histological study (Delafield, 1984).

2.8. Biochemical Analysis

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) liver enzyme activities were measured in serum by the method of Reitman and Frankel (1957).

2.9. Statistical Analyses

Statistical analyses were performed with SPSS 16 software. The experimental data were analyzed using one-way analysis of variance (ANOVA). The Duncan's multiple range test was used to determine the significant differences between means. All values were expressed as mean ± SD, and the significance level was set at $P \leq 0.05$.

3. Results and Discussion

3.1. Sesame Oil Analyses

3.1.1. Fatty Acids

The fatty acid composition is an essential indicator of the dietary nutritional value of the oil. As summarized in Table 1, the main fatty acids in SO are palmitic (13.57±2.71), stearic (4.23±0.41), oleic (42.93±3.76) and linoleic (35.77±2.21) in addition to some traces of palmitoleic (0.67±0.25), heptadecanoic (0.43±0.20), linolenic acid (0.73±0.40), arachidic (0.87±0.20) and eicosenoic (0.77±0.15). Hassan (2012) revealed that sesame oil belongs to the oleic–linoleic acid group. It has less than 20 % saturated fatty acid consisting mainly of palmitic and stearic acids. Oleic acid and linoleic acid constitute more than 80 % of the total fatty acids in the sesame seed oil. It has been mentioned that edible oil fatty acids may exert beneficial health effects by the modulation of signaling pathways regulating cell differentiation and proliferation (Lewinska *et al*., 2015).

3.1.2. Phenolic and Vitamin E Content

Sesame seeds are a rich source of antioxidants and bioactive compounds including phenolics. In addition, among the vitamins of sesame seeds, vitamin E is very essential which makes sesame seeds efficient as healthy food (Pathak *et al.*, 2014). The analysis of sesame oil revealed that SO's phenolic and vitamin E content was (15±2.0) and (6.77±0.77), respectively as shown in Table 1.

3.1.3. Antioxidant Activity

The antioxidant activity measurement showed that sesame oil at 200 µL exhibited an antioxidant activity of 61.03±0.74 as shown in Table 1. Previous studies revealed that the sesame oil possesses a strong antioxidant activity that greatly boosted its applications in the healthy food products because of its efficiency in the protection of the liver and the heart. In fact, sesame oil can be classified as edible oil with a high potential of antioxidant activity (Cheng et al., 2006; Bopitiya and Madhujith, 2013).

Table 1. Chemical composition and antioxidant activity of sesame oil.

Parameters	**Value**
Fatty acids	**(%)**
Palmitic	13.57±2.71^{c}
Palmitoleic	0.67±0.25^{de}
Heptadecanoic	0.43±0.20^{de}
Stearic	4.23±0.41^{d}
Oleic	42.93±3.76^{a}
Linoleic	35.77±2.21^{b}
Linolenic	0.73±0.40^{de}
Arachidic	0.87±0.20^{de}
Eicosenoic	0.77±0.15^{de}
Total phenolic content (mg gallic acid /100g oil)	15.00±2.00
Vitamin E concentration (µg/mL)	6.77±0.77
Percentage of antioxidant activity (200 uL)	61.03±0.74

Data are expressed as means ± SD. Mean values in the same column within each parameter bearing the same superscript do not differ significantly ($P \leq 0.05$).

3.2. Relative Liver Weight

3.2.1. Effects of BPA on Relative Liver Weight

According to the data in Table 2, the oral administration of BPA to male mice at a dose of 50 mg/kg b wt for twenty-eight consecutive days caused a significant decrease ($p \leq 0.05$) in the relative liver weight (3.19±0.05) compared to the control (3.38±0.05). These results are in agreement with the findings of Hassan *et al.* (2012) who demonstrated that the oral administration of BPA to male rats at the dose of 0.1 mg/kg/day for four weeks induced a significant decrease in the body weight compared to the control. In addition, previous data demonstrating that exposure to BPA during embryo development and infancy decreased the organ weights of male mice and rats (Kabuto *et al.*, 2004; Gamez *et al.*, 2014).

3.2.2. The Protective Effect of SO against the BPA Effect on Relative Liver Weight

The relative weight of liver of the male mice treated with BPA and SO are summarized in Table 2. Results showed that the oral administration of SO according to the three regimens of treatment caused a significant increase ($P \leq 0.05$) in the relative weight of liver compared with the BPA-treated male mice. These results are in agreement with Hussien *et al.* (2013) who reported that the administration of SO with cypermethrin resulted in significant protection against its toxicity on body and organ weights of rats.

Table 2. Means and standard deviations of relative liver weight of male mice treated with BPA and/or SO for 28 consecutive days.

Treatments	Relative liver weight(g/100g)
Control	3.38±0.05^{ab}
Vehicle	3.39±0.05^{a}
SO	3.41±0.04^{a}
BPA	3.19±0.05^{d}
SO before BPA	3.34±0.06^{abc}
SO with BPA	3.28±0.10^{c}
SO after BPA	3.30±0.05^{bc}

Data are expressed as means ± SD. Mean values in the same column within each parameter bearing the same superscript do not differ significantly ($P \leq 0.05$).

3.3. Genetic Investigation

3.3.1. BPA's DNA Damage

As shown in Table 3, the mean values of tailed cells, tail length, tail DNA percentage and olive tail moment in liver cells of male mice treated with BPA were significantly increased than the control. These results came to a consensus with Tiwari *et al.* (2012) who found a significant increase in the micronuclei occurrence, structural chromosomal aberrations in the cells of bone marrow and DNA damage in the lymphocytes of adult rats treated with BPA in various doses (10 µg, 5 mg and 50 mg/kg b wt). In addition, a significant increase in the levels of chromosome aberrations and DNA damage in Chinese hamster ovary (CHO) cells exposed to BPA was observed by Xin *et al.* (2015). The alkaline comet assay is utilized in different research areas as a quantitative and qualitative technique to measure the DNA strand breaks in the cells (Gedik et al., 1998). The mechanism of BPA genotoxicity might work through the oxidative stress induction and the depletion of antioxidant enzymes (Meeker *et al.*, 2010). In addition, the micronuclei induction might be attributed to the BPA aneugenic effect (Hunt *et al.*, 2003; Quick *et al.*, 2008).

3.3.2. The Protective Effects of SO against BPA's DNA Damage

Significant alleviation ($P \leq 0.05$) in the mean values of tailed cells, tail length, DNA percentage in tail and olive tail moment as a result of the SO administration through the three regimens of treatment was observed (Table 3). In addition, data clearly illustrated that the treatment of mice with SO before BPA was the best regimen in restoring the observed DNA alterations (in liver tissue) followed by the administration of SO after the BPA treatment whereas, the co-administration of both SO and BPA was the least effective.

Several studies are in harmony with these results, Chattopadhyay *et al.* (2010) who revealed that the co-administration of sesame lignans and nicotine tartrate for fifteen days minimized the percentage of nicotine DNA damage in rat liver. Arumugam and Ramesh (2011) demonstrated that pretreatment with SO showed reduction in DNA damage induced by 4-Nitroquinoline-1-oxide. In addition, Hussien *et al.* (2013) found that the treatment of female rats with SO and cypermethrin together for thirty consecutive days obviously alleviated the incidence of DNA damage in brain tissues**.**

The SO protective effects could be attributed to its lignans compounds namely sesamol, sesamin and sesaminol (Suja *et al.*, 2004), which are responsible for many of the physiological and biochemical properties as antimutagenic and antioxidant (Rong *et al.*, 2005). In addition, these results might be attributed to the antioxidant nature of phenolic compounds in the SO, which have antimutagenic, anticarcinogenic, and anti-inflammatory properties that might potentially be helpful in caring for the genome stability (Xie *et al.*, 2013).

Table 3. Comet assay parameters in liver cells of treated male mice with BPA and/or SO for 28 consecutive days

Treatments	Tailed cells (%)	Tail length (µm)	Tail DNA (%)	Olive tail moment (µm)
Control	12.00±1.00^{e}	7.66±0.80^{e}	13.53±0.51^{d}	1.03±0.08^{d}
Vehicle	12.73±0.54^{de}	8.56±0.41^{e}	13.15±0.22^{d}	1.12±0.04^{d}
SO	12.67±0.57^{de}	8.40±0.45^{e}	13.50±0.26^{d}	1.13±0.05^{d}
BPA	29.43±0.51^{a}	17.30±1.08^{a}	19.93±0.58^{a}	3.63±0.52^{a}
SO before BPA	14.00±1.00^{d}	11.26±0.30^{d}	15.03±0.25^{c}	1.70±0.06^{c}
SO with BPA	18.67±0.55^{b}	13.93±0.31^{b}	16.76±1.50^{b}	2.20±0.14^{b}
SO after BPA	17.00±1.00^{c}	12.90±0.10^{c}	15.16±0.47^{c}	1.95±0.05^{bc}

Data are expressed as means ± SD. Mean values in the same column within each parameter bearing the same superscript do not differ significantly ($P \leq 0.05$).

3.4. Histopathological Examination

3.4.1. BPA's Histopathological Alterations

Oral administration of BPA for twenty-eight consecutive days caused several histopathological alterations in the liver of male mice. The examination of the mice liver sections treated with BPA revealed marked congestion of the hepatic blood vessels as well as marked vacuolar degeneration of the hepatocytes with many necrotic cells (Figure 1 B and C). The investigation of histopathological alterations in the liver treated with BPA, established the genetic findings as well. These data are confirmed by Korkmaz *et al.* (2010) who noticed hepatic necrosis and congestion in male rats submitted to BPA treatment (25 mg/kg/day) for 50 day. Moreover, Ahmed *et al.* (2015) found that the treatment with BPA of adult male rats at the dose of 150 mg/kg for seventy consecutive days caused hepatic histopathological alterations.

These histopathological alterations may be related to the induction of DNA damage by BPA in these tissues. Moreover, it has been reported that BPA can cause oxidative damage in rat organs by generating ROS (Chitra *et al.*, 2002; Kabuto *et al.*, 2004). In addition, Sangai and Verma (2012) found that BPA caused changes in the activities of ATPase in the liver and kidney of mice thereby causing a reduction in the ATP production which causes necrosis.

3.4.2. The Protective Effects of SO against BPA's Histopathological Alterations

The microscopical examination of liver tissues revealed that SO through the three regimens of treatment with BPA

effectively improved the histological alterations induced by BPA especially the regimen of administration of SO before the BPA treatment. Liver histopathological examination of the SO-treated mice for twenty-eight successive days before the BPA treatment showed a mild degree of hepatocellular degeneration and necrosis (Figure 1 D). While, liver sections of the mice co-treated with SO and BPA showed centrilobular necrosis and degeneration of the hepatic cells (Figure 1 E). The examination of the liver sections of SO-treated mice for twenty-eight successive days after the BPA treatment showed congestion of the central veins and blood vessel moderate necrobiotic in the hepatocytes (Figure 1 F).

These findings are in agreement with those of Periasamy *et al.* (2012) who confirmed the protective effects of SO against monocrotaline-induced liver histopathological changes in rats. In addition, Soliman *et al.* (2015) noticed that the treatment of rats with SO ameliorated cypermethrin induced degenerative changes in the liver tissue. The protective role of SO may be attributed to the antioxidant nature of vitamin E that can prevent cell oxidative damage by preventing the oxidation of unsaturated fatty acids (Kim *et al*., 2012). In addition, SO contains active phenolic lignans such as sesamin, sesamol, and sesamolin, which are known as hepato-protective components (Periasamy *et al.*, 2014).

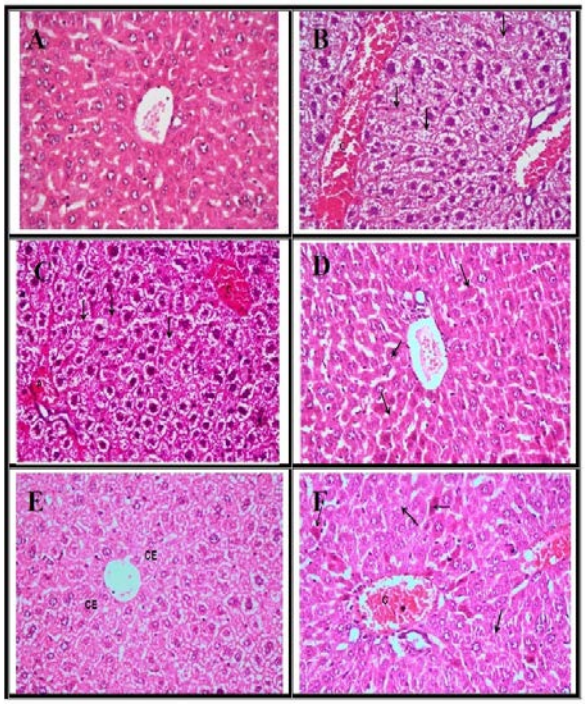

Figure 1. (A) Liver of control mice appearing within normal limits. B & C) Liver of BPA- treated mice showing hepatic blood vessels congestion (C), marked vacuolar degeneration of the hepatocytes with many necrotic cells (arrow), congestion of the central vein (C) and portal blood vessels (P) with marked hepatocellular vacuolar degeneration and necrosis (arrow). D) Liver of SO-treated mice before BPA showing mild degree of hepatocellular degeneration and necrosis (arrow). E) Liver of SO-treated mice concurrently with BPA showing centrilobular (CE) necrosis and degeneration of the hepatic cells. F) Liver of SO-treated mice after BPA treatment showing congestion (C) of the portal blood vessels and hepatocytes moderate necrobiotic changes (thick arrow) in the hepatocytes, Notice apoptotic cells (thin arrow) (H&E X400).

3.5. Biochemical Analysis

Finally, to confirm the protective effects of SO against the histopathological alterations induced by BPA in the liver tissue, serum AST and ALT were determined.

3.5.1. The Effects of Bisphenol A on Liver Enzymes

Results in Table 4 showed that the oral administration of BPA caused a significant increase ($P \leq 0.05$) in serum AST (49.33±1.52) and ALT (42.33±1.52) levels compared to control (29.67±1.15 and 24.67±1.15, respectively). These findings are in conformity with Korkmaz *et al.* (2010) who revealed that aspartate transaminase (AST) and alanine transaminase (ALT) levels were increased in male rats exposed to BPA (25 mg/kg) for fifty days. The high level of AST and ALT was accompanied by free radical generation and alteration in the liver tissue (Gaskill *et al.*, 2005).

3.5.2. Sesame Oil Protective Effects against BPA's Liver Dysfunction

Compared to the BPA group, the oral administration of SO through the three regimens of treatment with BPA significantly attenuated the liver enzymes (Table 4). Furthermore, the treatment of mice with SO at regimen before the BPA administration resulted in the best alleviation of the serums ALT and AST levels followed by the administration of oil at regimen after and during the BPA treatment. These findings are in accordance with Periasamy *et al.* (2012) who reported that SO significantly alleviated the AST and ALT levels in monocrotaline-treated rats.

Table 4. Biochemical measurements in the serum of BPA and/or SO treated male mice for 28 consecutive days.

Treatments	AST(U/L)	ALT(U/L)
Control	29.67±1.15 ^{de}	24.67±1.15^{c}
Vehicle	31.00±2.00^{cde}	23.67±0.57^{c}
SO	27.33±0.57^{e}	24.67±1.15^{c}
BPA	49.33±1.52^{a}	42.33±1.52^{a}
SO before BPA	32.00±1.73^{cd}	27.67±3.51^{c}
SO with BPA	41.00±2.64^{b}	34.67±2.08^{b}
SO after BPA	34.33±4.50^{c}	27.68±5.03^{c}

Data are expressed as means ± SD. Mean values in the same column within each parameter bearing the same superscript do not differ significantly ($P \leq 0.05$).

4. Conclusion

It can be concluded that BPA has the potential to produce genotoxic effects, and histopathological alterations in the liver tissue of male mice in addition to biochemical alterations. Accordingly, strict limitations on the use of this compound must be put especially in food contact materials. Sesame as a valuable seed oil appears to have abundant beneficial properties for applications in food. In addition, it can be considered as an excellent novel and multi-purpose ingredient in several industrial, cosmetic, and pharmaceutical products. Data reported herein illustrated that sesame seed oil can used as an antioxidant to attenuate the hepatotoxicity of BPA. Subsequently, it can be

categorized as edible oil with a high potential of antioxidant activity.

References

Ahmed WMS, Moselhy WA and Nabil TM. 2015. Bisphenol- A toxicity in adult male rats: hematological, biochemical and histopathological approach. *Glob Vet*, **14 (2):** 228-238.

AOAC.2000. **Association of Official Analytical Chemists. Official Methods of Analysis**. 17th ed. Gaithersburg, M.D. U.S.A.

Arumugam P and Ramesh S. 2011. Protective effects of sesame oil on 4-NQO-induced oxidative DNA damage and lipid peroxidation in rats. *Drug Chem Toxicol*, **34 (2):** 116-119.

Azab AE. 2014. Hepatoprotective effect of sesame oil against lead induced liver damage in albino mice: Histological and biochemical studies. *Am J Biosci*, **2**: 1-11.

Bandyopadhyaya G, Sinha S, Chattopadhyay BD and Chakraborty A. 2008. Protective role of curcumin against nicotine-induced genotoxicity on rat liver under restricted dietary protein. *Eur J Pharmacol*,, **588**: 151–157.

Biedermann S, Tschudin P and Grob K. 2010. Transfer of bisphenol A from thermal printer paper to the skin. *Anal Bioanal Chem*, **398:** 571–576.

Bindhumol V, Chitra KC and Mathur PP. 2003. Bisphenol A induces reactive oxygen species generation in the liver of male rats. *Toxicol*, **188**: 117–124.

Bopitiya D. and Madhujith T. 2013. Antioxidant activity and total phenolic content of Sesame (*Sesamum indicum* L.) seed oil. *Trop Agr Res*, **24 (3):** 296 – 302.

Cengiz N, Kavak S, Guzel A, Ozbek H, Bektas H ¸ Him A, Erdogan E, Balahoroglu R. 2013. Investigation of the hepatoprotective effects of sesame (*Sesamum indicum* L.) in carbon tetrachloride-induced liver toxicity. *J Membrane Biol*, **246:**1–6

Chattopadhyay K, Mondal S, Chattopadhyay B and Ghosh S. 2010. Ameliorative effect of sesame lignans on nicotine toxicity in rats. *Food Chem Toxicol*, **48:** 3215–3220.

Cheng FC, Jinn TR, Hou RC, Tzen JT. 2006. Neuroprotective effects of sesamin and sesamolin on gerbil brain in cerebral ischemia. *Int J Biomed Sci*, **2**:284–288.

Chitra KC, Latchoumycandane C and Mathur PP . 2002. Effect of nonylphenol on the antioxidant system in epididymal sperm of rats. *Arch of Toxicol*, **76**: 545–551.

Delafield F. 1984. **Haematoxylin and Eosin for General Staining. Staining of the Animal Tissues Practical and Theoretical**. London, Oxford University Press.

Doherty L, Bromer J, Zhou Y, Aldad T and Taylor H. 2010. In utero exposure to diethylstilbestrol (DES) or bisphenol-A (BPA) increases EZH2 expression in the mammary gland: anepigenetic mechanism linking endocrine disruptors to breast cancer. *Horm Cancer*, 1**(3):** 148–155.

Erler C and Novak J. 2010. Bisphenol A exposure: human risk and health policy. *J Pediatr Nurs*, **25**: 400–407.

Erol AYG, Bulbul A, Avci G, Ozdemir M and Akkaya O. 2011. The protective effects of omega-3 fatty acids and sesame oil on cyclosporine-A induced liver apoptosis. *J Acad Res Med*, **1**: 8-11.

Flint S, Markle T, Thomson S and Wallace E. 2012. Bisphenol A exposure effects and policy; a wildlife perspective. *J Environ Manage*, **104**: 19–34.

FukudaY. 1990. Food chemical studies on the antioxidants in sesame seed. *Nippon Shokuhin Kogyo Gakkaishi*, **37**: 484-492.

Gamez JM, Penalba R, Cardoso N, Ponzo O, Carbone S, Pandolfi M, Scacchi P and Reynoso R . 2014. Low dose of bisphenol A impairs the reproductive axis of prepuberal male rats. *J Physiol Biochem*, **70**: 239–246.

Gaskill CL, Miller LM and Mattoon JS . 2005. Liver histopathology and liver and serum alanine aminotransferase and alkaline phosphatase activities in epileptic dogs receiving phenobarbital. *Vet Pathol*, **42(2):** 147-160.

Gassara F, Brar SK, Verma M and Tyagi R. 2013. Bisphenol A degradation in water by ligninolytic enzymes. *Chemosphere*, **92**:1356–1360.

Gedik CM, Wood SG and Collins AR. 1998. Measuring oxidative damage to DNA: HPLC and the comet assay compared. *Free Radic Res*, **29:** 609–615.

Gimeno E, Castellote AI, Lamuela-Raventos RM, Torre MC and Lopez-Sabater MC. 2000. Rapid determination of vitamin E in vegetable oils by reversed phase high-performance liquid chromatography. *J Chromatogr A*, **881**: 251–254.

Hassan AM . 2012. Studies on Egyptian sesame seeds (*Sesamum indicum* L.) and its products 1–physicochemical analysis and phenolic acids of roasted Egyptian sesame seeds (*Sesamum indicum* L.).*World J. Dairy Food Sci*, **7 (2):** 195-201.

Hassan ZK, Elobeid MA, Virk P, Omer SA, ElAmin M, Daghestani MH and Al Olayan EM . 2012. Bisphenol A induces hepatotoxicity through oxidative stress in rat model. *Oxidative Med Cellular Longevity*, **2012:** 1-6.

Hoekstra E and Simoneau C . 2013. Release of bisphenol A from polycarbonate-a review. *Critic Rev Food Sci Nutri*, **53**: 386–402.

Hunt PA, Koehler KE, Susiarjo M, Hodges CA, Ilagan A, Voigt RC, Thomas S, Thomas BF and Hassold TJ. 2003. Bisphenol a exposure causes meiotic aneuploidy in the female mouse. *Current Biol*, **13**: 546–553.

Hussien HM, Abdou HM and Yousef MI . 2013. Cypermethrin induced damage in genomic DNA and histopathological changes in brain and haematotoxicity in rats: The protective effect of sesame oil. *Brain Res Bull*, **92**: 76– 83.

Kabuto H, Amakawa M and Shishibori T . 2004. Exposure to bisphenol A during embryonic/fetal life and infancy increases oxidative injury and causes underdevelopment of the brain and testis in mice. *Life Sci*, **74**: 2931–2940.

Kim M, Kim E, Kim YN, Choi C and Lee C. 2012. Comparison of the chemical composition and nutritive values of various pumpkin (Curbitaceous) species and parts. *Nutr Res Pract*, **6(1):** 21-27.

Korkmaz A, Ahbab MA, Kolankaya D and Barlas N . 2010. Influence of vitamin C on bisphenol A, nonylphenol and octylphenol induced oxidative damages in liver of male rats. *Food Chem Toxicol*, **48(10):** 2865-2871.

Lee M, Kwon J and Chung M . 2003. Enhanced prediction of potential rodent carcinogenicity by utilizing comet assay and apoptotic assay in combination. *Mut Res*, **541**: 9–19.

Lewinska A, Zebrowski J, Duda M, Gorka A and Wnuk M. 2015. Fatty Acid profile and biological activities of linseed and rapeseed oils. *Molecules*, **20**:22872–22880

Lin JY and Tang CY. 2007. Determination of total phenolic and flavonoid contents in selected fruits and vegetables, as well as their stimulatory effects on mouse splenocyte proliferation. *Food Chem*, **101**: 140–147.

Maffini MV, Rubin BS, Sonnenschein C and Soto AM . 2006. Endocrine disruptors and reproductive health: the case of bisphenol-A. *Mol Cell Endocrinol*, **254– 255**: 179–186.

Meeker JD, Ehrlich S, Toth TL, Wright DL, Calafat AM, Trisini AT, Ye X and Hauser R . 2010. Semen quality and sperm DNA damage in relation to urinary Bisphenol A among men from an infertility clinic. *Reprod Toxicol*, **30**: 532–539.

Michalowicz J. 2014. Bisphenol A- sources, toxicity and bio-transformation. *Environ Toxicol Pharmacol*, **37**: 738–758.

Pathak N, Rai AK, Kumari R and Bhat KV. 2014.Value addition in sesame: A perspective on bioactive components for enhancing utility and profitability. *Pharmacogn Rev*, **8(16):**147–155.

Periasamy S, Hsu DZ, Chang PC and Liu MY. 2014. Sesame oil attenuates nutritional fibrosing steatohepatitis by modulating matrix metalloproteinases-2, 9 and PPAR-γ. *J Nutr Biochem*, **25**: 337–344.

Periasamy S, Yang SS, Chen SY, Chang CC and Liu MY. 2012. Prophylactic sesame oil attenuates sinusoidal obstruction syndrome by inhibiting matrix metalloproteinase–9 and oxidative stress. *J Parenter and Enteral Nutr*, 37 **(4):** 529-537.

Quick EL, Parry EM and Parry JM . 2008. Do oestrogens induce chromosome specific aneuploidy *in vitro*, similar to the pattern of aneuploidy seen in breast cancer. *Mut Res*, **651**: 46–55.

Reitman S and Frankel S. 1957. Glutamic–pyruvate transaminase assay by colorimetric method. *Am J Clin Path*, **28**: 56.

Rong CP, Liong CK, Chen ST, Jen CC, Liu TL and Cheng H . 2005. Dietary sesame reduces serum cholesterol and enhances antioxidant capacity in hypercholesterolemia. *Nutr Res*, **25**: 559-567.

Sangai NP and Verma RJ . 2012. Effect of quercetin on bisphenol A-caused alterations in succinate dehydrogenase and adenosine triphosphatase activities in liver and kidney of mice. *Acta Poloniae Pharmaceutica- Drug Res*, **69(6):** 1189-1194.

Sankar D, Sambandam G, Ramakrishna RM and Pugalendi KV . 2005. Modulation of blood pressure, lipid profiles and redox status in hypertensive patients taking different edible oils. *Clin Chim Acta*, **355**: 97–104.

Singh RP, Murthy KN and Jayaprakasha GK .2002. Studies on the antioxidant activity of pomegranate *(Punica granatum)* peel and seed extracts using *in vitro* models. *J Agric Food Chem*, **50**: 81-86.

Soliman MM, Attia HF and Abou El-Ella GA .2015. Genetic and histopathological alterations induced by cypermethrin in rat kidney and liver: Protection by sesame oil. *Int J Immunopathol Pharmacol*, **28 (4):** 508-520.

Srinivasan P and Liu MY. 2012. Comparative potential therapeutic effect of sesame oil and peanut oil against acute monocrotaline (*Crotalaria*) poisoning in a rat model. *J Vet Intern Med*, **26**: 491–499.

Suja KP, Jayalekshmy A and Arumughan C .2004. Free radical scavenging behavior of antioxidant compounds of sesame (*Sesamum indicum* L.) in DPPH system. *J Agric Food Chem*, **52**: 912-915.

Tiwari D, Kamble J, Chilgunde S, Patil P, Maru G, Kawle D, Bhartiya U, Joseph L and Vanage G . 2012. Clastogenic and mutagenic effects of bisphenol A: an endocrine disruptor. *Mut Res*, **743**: 83–90.

Xie C, Wang C, Wang X and Yang X . 2013. Two modified RNA extraction methods compatible with transcript profiling and gene expression analysis for cotton roots. *Prep Biochem Biotechnol*, **43(5):** 500-511.

Xin L, Lin Y, Wang A, Zhu W, Liang Y, Su X, Hong C, Wan J, Wang Y and Tian H . 2015. Cytogenetic evaluation for the genotoxicity of bisphenol-A in Chinese hamster ovary cells. *Environ Toxicol Pharmacol*, **40**: 524–529.

Zeinab K, Hassan Z, Elobeid M, Virk P, Omer S, ElAmin M, Daghestani M, Ebtisam M and Al Olayan E . 2012. Bisphenol A induces hepatotoxicity through oxidative stress in rat model. *Oxid Med and Cell Longev*, **2012**:1-6.