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The Effects of *Panax ginseng* on Serum Oxidative Stress Following Bisphenol A Exposure

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ABSTRACT

Objective: Bisphenol A (BPA) is a toxic compound that causes oxidative stress by disrupting antioxidant enzymes and promoting tissue lipid peroxidation. This study aimed to examine the impacts of BPA on serum oxidative stress in rats and to detect the antioxidant feature of *Panax ginseng* (PxG) in reducing BPA-induced oxidative stress.

Materials and Methods: Wistar Albino rats (250-300 g) were divided into control, control + PxG, BPA, and BPA + PxG groups. 50 mg/kg BPA and 100 mg/g PxG were given for six weeks. Serum total antioxidant and oxidant status, lipid peroxidation, and glutathione levels were determined.

Results: BPA administration increased total oxidant status and lipid peroxidation, while PxG administration to the BPA group decreased these parameters. PxG also increased total antioxidant status and glutathione levels compared to the BPA group.

Conclusion: BPA was seen to cause an increase in oxidative parameters and PxG administration to restore the oxidative stress that was generated after BPA exposure, suggesting that this may help to prevent the adverse effects caused by BPA exposure.

Keywords: Bisphenol A, *Panax ginseng*, oxidative stress, antioxidant effect

INTRODUCTION

Bisphenol A (BPA), is an industrial product produced in most plastic manufacturing industries (1), and causes oxidative stress by suppressing antioxidant levels and increasing lipid peroxidation and free radicals (2). BPA is a toxic monomer that damages DNA through an oxidative process (3). A relationship exists between BPA consumption and a high risk of kidney impairment and liver damage (4). BPA-associated oxidative stress leads to the disruption of cellular homeostasis, which causes inflammation and tissue damage responses (5). Apart from the liver and kidneys, BPA has been linked to a number of other health problems due to oxidative stress, such as heart-related diseases (4), and metabolic disorders (1), which suggests the far-reaching nature of this chemical regarding all aspects of human health.

Because research on the properties of traditional plants has revealed many bioactive compounds to reduce oxidative

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damage or strengthen the antioxidant system, the tendency toward natural compound research has increased. *Pistacia integerrima* (6), grape seed (7), sweet potato (8), Tualang honey (9), and sesame lignans (10) have been demonstrated to have preventive benefits regarding tissue damage caused after BPA exposure. The present study investigated the possible effects of *Panax ginseng* (PxG) on BPA-induced oxidative stress.

PxG, or Korean ginseng, is an enduring plant from the Araliaceae family (11) and grows mainly in East Asia and North America (12). It contains several bioactive molecules including ginsenosides, polyphenols, and phytosterol, which play a significant role in certain pharmacological effects (13, 14). Ginsenosides have potent antioxidant effects and can inhibit oxidative damage. Ginsenosides' reactive oxygen species scavenging properties are responsible for their protective action (13). PxG has been shown to have a regulating effect on blood glucose levels, offering protection from cardiovascular risk factors (14), as well as to improve cognitive function, physical tolerance (15), and sexual function (16).

An *in vitro* investigation has shown PxG to act as an anti-inflammatory on BPA-treated A549 lung cells by decreasing reactive oxygen species generation and affecting NF-κB activation and COX-2 expression (17). Ok et al. found ginseng to increase the anti-apoptotic mechanisms that inhibit BPA-induced apoptosis (18). Research on the influence of PxG administration regarding BPA-related abnormalities in the uterus and liver of ovariectomized mice has indicated PxG to protect these mice from chemotaxis generated by BPA and inflammatory reactions (19).

MATERIALS AND METHODS

Experimental Animal Model

Marmara University Animal Care and Use Ethics Committee approved the experimental stages of this study (Protocol Number: 57. 2023mar). The study used 32 rats (Wistar Albino, male), weighing an average of 250-300 grams. Conventional conditions were used throughout this stage. The rats were separated into Control (C), C + PxG, BPA, and BPA + PxG groups, with eight rats in each group. BPA was purchased from Sigma-Aldrich (Germany) and dissolved in 1% ethanol. PxG was obtained from Casel İlaç Sanayi A.Ş. (Turkiye) and dissolved in water.

The C group of rats were under a standard diet (BPA vehicle, orally). The C + PxG group was administered PxG (100 mg/kg, orally with BPA vehicle). The BPA group was administered 50 mg/kg BPA (orally). The BPA + PxG group was given BPA (50 mg/kg, orally, and 100 mg/kg of PxG, orally). BPA and PxG were administered to the rats for six weeks, five days per week. Trunk blood was used to prepare the serum samples.

Determining Serum Lipid Peroxidation and Glutathione (GSH)

For determining the lipid peroxidation, thiobarbituric acid makes a colorful complex with malondialdehyde (MDA) (20). The absorbance of the pink color resulting from the MDA-thiobarbituric acid reaction was measured by spectrophotometry. The GSH level was determined using the Beutler test (21), which involves reduction of Ellman's reagent with SH groups to generate yellow-colored 5, 5'-dithiobis (2-nitrobenzoic acid).

Determining the Serum Total Oxidant Status (TOS) and Antioxidant Status (TAS)

TOS and TAS were determined spectrophotometrically (RL No: 0017, RL No: 0024, respectively, Rel Assay Diagnostics, Gaziantep, Turkiye). The research used the antioxidant method to determine the ability of serum to counteract free-radical reactions and the oxidant measurement method to measure the ability of serum oxidants to change a ferrous ion to a ferric ion.

Oxidative Stress Index (OSI) Calculation

The following formula was utilized to calculate the OSI:

OSI = TOS (μmol H_2O_2 eq/L) / TAS (μmol Trolox eq/L)

Table 1: Serum TAS, TOS, and OSI Levels

	C	BPA	C+PxG	BPA+PxG	p-value
TAS (μmol/L)‡	1.78 ± 0.04	1.55 ± 0.09*,+■	2.31 ± 0.11*	2.25 ± 0.08*,+	0.0001
TOS (μmol/L)‡	5.80 ± 0.22	10.95 ± 0.39*,+■	4.37 ± 0.30*	4.72 ± 0.29*,+	0.0001
OSI‡	0.034 ± 0.002	0.075 ± 0.005*,+■	0.019 ± 0.002*	0.021 ± 0.003*,+	0.0001

C: control group; BPA: BPA exposed group; C + PxG: control + Panax ginseng group; BPA + PxG: BPA exposed + Panax ginseng administered group; TAS: total antioxidant status; TOS = total oxidant status; OSI = oxidative stress index

*Compared to the C group;

+Compared to the BPA group;

■ Compared to the BPA + PxG group;

‡: Mean ± SD

Statistical Analyses

GraphPad Software (GraphPad Prism 9.0, California, USA) was used to conduct the statistical analysis, with means and standard deviations (SD) being used to present the data. Analysis of variance (ANOVA) and the post hoc Tukey test were used to compare the groups, with a $p < 0.05$ being accepted as significant.

RESULTS

TAS, TOS, and OSI Levels

BPA administration decreased TAS and increased TOS and OSI significantly, compared to the C group (Table 1). PxG administration significantly increased total antioxidant status, significantly decreased TOS, and reduced OSI, compared to the C group (Table 1). When compared to the BPA group, the BPA + PxG group showed a significant increase in total antioxidant status and a significant reduction in TOS and OSI.

MDA and GSH Levels

According to Figure 1, administering BPA to the C group increased MDA levels significantly, and administering PxG to the BPA group decreased their MDA levels. In addition, MDA levels in the BPA + PxG group increased significantly compared to the C + PxG group (Figure 1). Applying BPA to the rats did not change their GSH levels (Figure 1). Administering PxG to the C group and BPA groups significantly increased the GSH levels in both groups (Figure 1).

DISCUSSION

The widespread use of BPA and its potential health consequences are still being researched. This study has determined the possible effects of BPA on health, especially its potential effects on serum oxidative stress, and also determined the role of PxG, primarily its antioxidant properties, on these effects.

The excessive generation of free radicals causes peroxidative alterations, which eventually result in increased lipid peroxidation, which could be used used as a diagnostic indicator of tissue damage (22). Many studies have highlighted how BPA damages tissues through oxidative stress (23, 24). Ge et al. found BPA to restrict the growth of Sertoli cells by causing oxidative stress, whereas low-dose BPA promotes cell growth by stimulating the metabolism with regard to energy (25). Tiwari et al. found that, although BPA is not carcinogenic, it does have genotoxic effects (26). Similar to these studies, administering BPA to rats in the current study increased their serum lipid peroxidation levels and oxidative stress. Compared to the results presented by Ozaydin et al. and Moghaddam et al., which revealed a decrease in GSH levels in BPA-exposed groups (24, 27), this study detected no significant changes in serum GSH levels after BPA exposure. The lack of change in serum GSH levels following BPA administration indicates that the body may metabolize BPA through different detoxification pathways. As a traditional medicine that has been used for centuries, PxG is an Asian plant with an antioxidant potential due to its ginsenoid content. PxG could assist in the 'body's

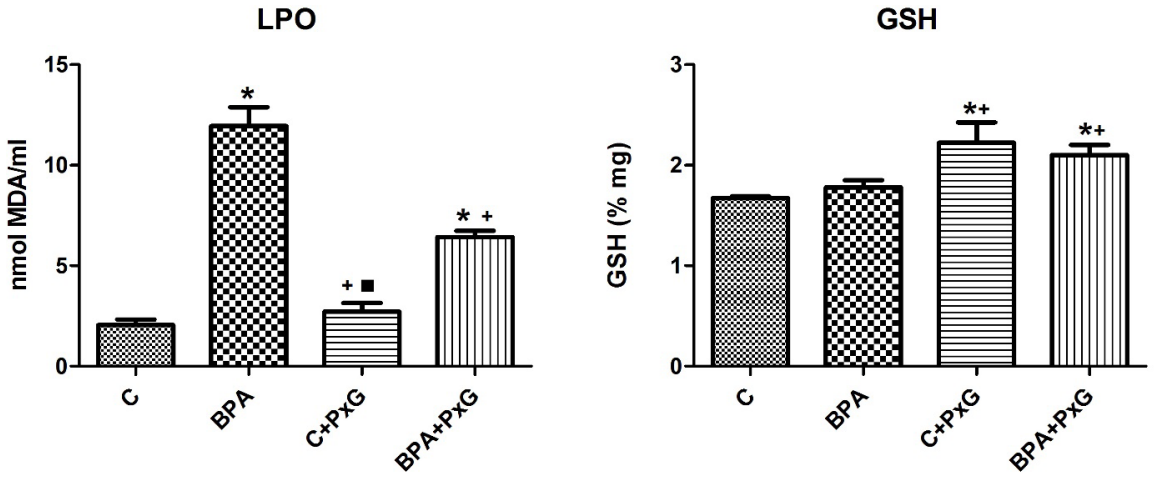

Figure 1. Serum MDA and GSH levels.
C: control group; BPA: BPA exposure group; C + PxG: control + Panax ginseng group; BPA + PxG: BPA exposure + Panax ginseng administered group; MDA: malondialdehyde; LPO: lipid peroxidation; GSH: glutathione.
* Compared to the C group;
+ Compared to the BPA group;
■ Compared to the BPA + PxG group

neutralization of free radicals, thus preventing cells from oxidative damage. Kim et al. showed PxG to reduce serum lipid peroxidation and to increase antioxidant enzyme activities after exercise-induced oxidative stress (28). Ramesh et al. have shown PxG to ameliorate age-related oxidative damage in tissues (29). Chung et al. demonstrated PxG to significantly increase the total antioxidant capacity in postmenopausal women (30). Consistent with these studies, the current study has shown PxG to increase serum TAS and GSH levels in rats exposed to BPA, while decreasing TOS and lipid peroxidation. This highlights the possible anti-oxidative capacity of PxG for reducing BPA-induced oxidative stress. The study has also showed administering PxG to healthy rats to also increase TAS and GSH levels, suggesting potential protective effects of PxG against oxidative stress.

In conclusion, PxG can decrease BPA-induced oxidative damage and may potentially be an efficient protector against other environmental contaminants. Because of its antioxidant properties, PxG may prove useful in treating oxidative stress-related diseases.

Ethics Committee Approval: Marmara University Animal Care and Use Ethics Committee approved the experimental stages of this study (Protocol Number: 57. 2023mar).

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Conflicts of Interests: The authors declare that they have no competing interests.

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