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Role of Quercetin against Polychlorinated Biphenyl (Aroclors 1242 and 1254) induced Changes in Biochemical Parameters and Antioxidant Status in Liver, Kidney, Brain, Heart and Testes of Rats

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Abstract:
Polychlorinated biphenyls (PCBs) are lipophilic environmental pollutants that have been found in practically every component of the world's ecosystem as contaminants. PCBs have been proven to induce lipid peroxidation via causing oxidative damage to biomolecules, antioxidant enzyme regulation, and oxidative stress. In this research, we looked into the effect of quercetin on the antioxidant status of PCBs(Aroclors 1242 and 1254)-induced toxicity in male rats. The protective role of quercetin (50 mg/kg body weight/day) was evaluated in the mixture of Aroclors 1242 and 1254-induced toxicity in rat blood, liver, kidney, brain, lung, heart, and testes. Animals were classified into four equal groups, control, quercetin (50 mg/kg BW), the mixture of Aroclors 1242 and 1254 (1:1, 2 mg/ kg body weight/day), and quercetin plus the mixture of aroclors, respectively. The respective doses of quercetin and the mixture of Aroclors were orally treated daily for 30 days. The mixture of aroclors induced an increase in plasma, liver, kidney, brain, lung, heart, and testes thiobarbituric acid reactive substances (TBARS), while the activities of antioxidant enzymes (GST, SOD, and GPx) were decreased. Transaminases and phosphatases were elevated in plasma and decreased in liver. Aroclors increased glucose, urea, and creatinine, while decreased immunoglobulin G (IgG), total protein, albumin, globulin, and bilirubin. Quercetin alone reduced TBARS, urea, creatinine, and bilirubin and increased antioxidant enzymes. The presence of quercetin with the mixture of Aroclors minimized its toxicity. In conclusion, administration of quercetin with 1242 and 1254 Aroclors mixture may alleviate its harmful effects.

INTRODUCTION

For more than 30 years, people have been becoming more conscious of the persistent toxic substances (PTS) threats to human health and the environment. Organic compounds are among the most dangerous substances because of their long-term stability in the environment, resistance to breakdown, and acute and chronic toxicity. These substances are incorporated and accumulated in the tissues due to their lipophilic character. These substances can cause major health and environmental problems, such as cancer and reproductive problems, changes in the developmental and immunological systems, as well as endocrine disturbance, provide a risk of reduced reproductive success, as well as the loss of biological variety in extreme circumstances (IOMC, 2002).

PCBs (polychlorinated biphenyls) are chemicals widely used in industry that are made up of 209 distinct compounds or congeners that have been commercially available since 1929. Under a wide range of chemical, thermal, and electrical conditions, PCBs are generally stable substances. PCBs bio-concentrate and bio-accumulate as a result of their lipophilic nature and stability, and are thus regularly identified in fatty tissues (Kimbrough and Jensen, 2012). Animal studies demonstrate a rise in liver tumors in rats and mice, as well as thyroid cancers in male rats exposed to various PCB combinations (Knerr and Schrenk, 2006). PCBs have been proved to cause oxidative stress (McCann *et al.*, 2021).

Although cells have mechanisms to defend themselves against toxic species, these defense systems deteriorate dramatically under physiological and environmental conditions that cause excessive production of reactive oxygen species (ROS), resulting in levels of oxidation that are unaffected by endogenous mechanisms (Bobadilla *et al.*, 2021). Therefore, additional dietary supplements with antioxidant nutrients are needed to protect against oxidative stress and the consequent pathologies such as atherosclerosis, ischemia, inflammation, cancer, cardiovascular disease, and neurological diseases (Bobadilla *et al.*, 2021).

Flavonoid molecules have been studied for their antioxidant activities, which appear to be linked to their protective activity against oxidative processes in many *in vivo* and *in vitro* models (Zeng *et al.*, 2020). Plasma antioxidant status has been shown to be significantly higher in quercetin-treated animals (Olayinka *et al*., 2015). Quercetin is the most abundant bioflavonoid found in vegetables and fruits (David *et al.,* 2016)**.** Therefore this study aimed to estimate the protective effect of quercetin as an antioxidant against the harmful effects of the mixture of polychlorinated biphenyls on biochemical and immunological indices.

MATERIAL AND METHODS

Chemicals and Doses

Aroclor 1254 (1,2,3-Trichloro-4-(2,3-dichlorophenyl)benzene), Aroclor 1242 (1,2-dichloro-3-(2,4-dichlorophenyl)benzene) and quercetin (2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one) dihydrate were obtained from Sigma Chemical Company, St Louis, MO, USA. The dose of polychlorinated biphenyls was used in this research according to Venkataraman et al. (2008) and Kunz *et al.* (2005) previous studies. On the other hand, quercetin dose was used based Morales et al. (2005) studies.

Animals and Treatments

Thirty two Wistar rats weighting 200 - 250 g were used. The animals used in this investigation were obtained from the Faculty of Agriculture at Alexandria University in Alexandria, Egypt. Animals were housed four to a cage and fed commercial diets and ad libitum tap water. After two weeks of adaptation, the rats were classified into four equal group. The first group served as a control group, while groups 2, 3 and 4 were treated with quercetin (50 mg/kg BW), the mixture of biphenyls 2 mg/kg BW (1 mg/kg BW of Aroclor 1254 and 1 mg/kg BW of Aroclor 1242; 1:1) and the combination of polychlorinated biphenyls and quercetin, respectively. Aroclor 1254 and Aroclor 1242 were dissolved in corn oil. Rats were orally

administered by gavage (stomach tube) their respective doses daily for one month. The dosage volume was 0.2 ml/100 gm BW rat.

Body weight and relative organs weight

The body weight of rats was measured at the end of the study. Animals were sacrificed by decapitation 24 hours after the last treatment, and the liver, lung, kidney, brain, heart, spleen, and testes were promptly removed and weighed, with the organs weight ratio computed. Organ relative weight (percentage) was computed using the formula g/100 g body weight.

Biochemical parameters

Plasma total protein (TP), albumin (A), glucose, urea, creatinine, total bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (AlP), and acid phosphatase (AcP) were measured using kits from Bio Systems S.A. Costa Brava, 30. 08030 Barcelona (Spain).

Liver, kidney, lung, brain, heart and testes glutathione S-transferase (GST), superoxide dismutase (SOD), glutathione peroxidase (GPx), and thiobarbituric acid-reactive substances (TBARS) were measured by the methods of Habig et al. (1974), Mishra and Fridovich (1972), Paglia and Valentine (1967), and Tappel and Zalkin (1959), respectively. Liver, kidney, lung, brain, heart and testes protein concentration was assayed using Lowrey et al. (1951) method. Plasma immunoglobulin G (IgG) was estimated by the methods of Engvall and Perlmann (1971) and Engvall (1977).

RESULTS

Body weight and organs relative weights

Table 1 represents the variations in body weight and relative weight of liver, kidney, brain, lung, heart, testes, epididymis, and spleen of male rats treated with quercetin, the mixture of polychlorinated biphenyls (PCBs; Aroclors 1242 and 1254) and their combinations. The results showed that quercetin treatment alone did not cause significant changes in body weight and the relative weights of liver, lung, testes, kidney, brain, heart, epididymis, and spleen. While, treatment with PCBs mixture alone decreased body weight and the relative weight of testes and increased the relative weights of liver, kidney and spleen. On the other hand, PCBs had no significant effect on the relative weights of heart, brain, lung, and epididymis. The presence of quercetin with the mixture of polychlorinated biphenyls minimized its toxic effect on body weight and organs weight.

Plasma protein

The mean values of plasma total protein (TP), albumin (A) and globulin (G) after 30 days experimental period are shown in Table 2. Treatment with quercetin alone increased TP, A, and G compared to control. While, treatment with the mixture of polychlorinated biphenyls resulted in a significant decrease in TP, A and G. The presence of quercetin with the mixture of polychlorinated biphenyls decreased its toxic effect and increased the reduction in TP, A and G.

Plasma glucose

Results illustrated that treatment with quercetin alone does not cause any change in plasma glucose. While, treatment with polychlorinated biphenyls alone caused a significant increase in plasma glucose compared to the control group. Rats treated with polychlorinated biphenyls in the presence of quercetin combinations indicated a significant decline in plasma glucose as compared with polychlorinated biphenyls group meaning that quercetin alleviated the toxic effect of polychlorinated biphenyls mixture (Table 2).

Bilirubin

The values of plasma bilirubin are shown in Table 2. Treatment with quercetin alone had no significant effect on plasma bilirubin. While, treatment with polychlorinated biphenyls mixture alone decreased plasma bilirubin. The presence of quercetin with polychlorinated biphenyls mixture decreased its toxic effect.

Plasma urea and creatinine

Results indicated that quercetin decreased creatinine while polychlorinated biphenyls mixture increased plasma urea and creatinine (Table 2). The presence of quercetin with PCBs mixture decreased its toxic effect.

Table 1. Body weight (BW) and relative weight of liver, kidney, brain, lung, heart, testes, epididymis, and spleen of male rats treated with quercetin, polychlorinated biphenyls (PCBs) mixture and their combinations.

Parameter	Experimental groups			
	Control	Quercetin	PCBs mixture	Quercetin+ PCBs mixture
BW (gm)	264±10.4^{a}	264±12.4^{a}	222±9.6^{b}	248±14.9^{ab}
Liver (g/100gm)	2.8±0.07^{b}	2.8±0.05^{b}	3.2±0.05^{a}	2.9±0.08^{b}
Kidney (g/100gm)	0.76±0.043^{ab}	0.69±0.022^{b}	0.85±0.038^{a}	0.74±0.089^{ab}
Brain (g/100 gm)	0.73±0.055^{a}	0.67±0.029^{a}	0.69±0.044^{a}	0.74±0.060^{a}
Lung (g/100 gm)	0.69±0.052^{a}	0.72±0.020^{a}	0.63±0.025^{a}	0.71±0.065^{a}
Heart (g/100 gm)	0.40±0.012^{a}	0.37±0.003^{a}	0.40±0.007^{a}	0.41±0.035^{a}
Testes (g/100 gm)	1.13±0.037^{a}	1.21±0.025^{a}	0.87±0.079^{b}	1.18±0.108^{a}
Epididymis (g/100 gm)	0.92±0.073^{a}	0.87±0.038^{a}	0.83±0.037^{a}	0.87±0.109^{a}
Spleen (g/100 gm)	0.45±0.046^{ab}	0.40±0.016^{b}	0.55±0.069^{a}	0.42±0.047^{ab}

Results are demonstrated as means ± SE; n = 8 for each treatment group

Mean values within a row not sharing a common superscript letters (a, b) were significantly different, $p<0.05$.

Table 2. Plasma biochemical parameters of male rats treated with quercetin, polychlorinated biphenyls (PCBs) mixture and their combinations.

Parameter	Experimental groups			
	Control	Quercetin	PCBs mixture	Quercetin+ PCBs mixture
Total protein (g/dl)	5.32±0.486^{a}	5.52±0.268^{a}	4.34±0.111^{b}	5.31±0.123^{a}
Albumin (g/dl)	3.72±0.051^{a}	3.85±0.234^{a}	3.13±0.106^{b}	3.71±0.154^{a}
Globulin (g/dl)	1.60±0.094^{a}	1.67±0.115^{a}	1.21±0.091^{b}	1.60±0.126^{a}
Glucose (mg/dl)	109.25±1.991^{b}	111.86±1.417^{b}	139.60±2.434^{a}	116.19±9.215^{b}
Bilirubin (mg/dl)	0.66±0.076^{a}	0.65±0.054^{a}	0.50±0.054^{b}	0.65±0.076^{a}
Urea (mg/dl)	42.13±1.136^{b}	43.19±3.380^{b}	51.70±1.148^{a}	45.25±1.524^{b}
Creatinine (g/dl)	0.94±0.068^{bc}	0.81±0.054^{c}	1.41±0.067^{a}	1.11±0.088^{b}

Results are demonstrated as means ± SE; n = 8 for each treatment group.

Mean values within a row not sharing a common superscript letters (a, b, c,) were significantly different, $p<0.05$.

Transaminases and phosphatases

Table 3 represents the mean values of the activities of aspartate transaminase (AST), alanine transaminase (ALT), acid phosphatase (AcP) and alkaline phosphatase (AlP) in plasma and liver of male rats treated with quercetin, PCBs mixture and their combinations. Results indicated that the exposure to quercetin alone did not affect plasma and liver AST, ALT, ALP and AcP activities. Whereas, exposure to PCBs mixture caused elevated plasma AST, ALT, ALP and AcP activities, while decreased in liver. The presence of quercetin with the mixture of PCBs minimized its toxic effect.

Thiobarbituric acid reactive substances and Antioxidant enzymes

Thiobarbituric acid reactive substances (TBARS) concentrations and the activities of glutathione S-transferase (GST), superoxide dismutase (SOD), and glutathione peroxidase (GPx) in plasma, liver, kidney, brain, lung, heart, and testes are expressed in Table 4. The presented

data showed that treatment with quercetin alone reduced the levels of TBARS in plasma, liver, testes, brain, kidney, heart, and lung. While, treatment with PCBs mixture significantly (p<0.05) increased the levels of TBARS in plasma and all tested organs. The presence of quercetin with PCBs mixture reduced the elevation in TBARS. Also, results showed that quercetin elevated GST, SOD, and GPx, but polychlorinated biphenyls (PCBs) mixture had significantly decreased them in plasma and all tested organs, while the combination overcame the oxidative effect of PCBs mixture.

Immunoglobulin G

Results showed that treatment with quercetin alone had no significant effect on the level of plasma IgG. Whereas, the mixture of polychlorinated biphenyls decreased it. The presence of quercetin with PCBs mixture decreased its immunosuppressive effect and increased the decrease in the level of plasma IgG of combination group (Table 5). The results obtained are consistent with Ross et al. (1996) who discovered that polychlorinated biphenyls are immunotoxic (decreased antibody production by erythrocytes in sheep and changes in the proportion of T helper and T suppressor cells) among treated monkeys. Meanwhile, Bugianesi et al. (2000) reported the accumulation of evidence emphasizing the importance of intracellular quercetin levels in maintaining immune functions. Lugli et al. (2009) suggested that quercetin cannot induce apoptosis in normal cells under various conditions, but it can impair the function of effector T cells, thus inhibiting normal immune function such as T cell proliferation and activation.

DISCUSSION

The decrease in body weight and relative testis weight (Table 1) is consistent with the results of Muthuvel et al. (2005) who suggested that weight loss may be due to reduced androgen availability and production in rats exposed to Aroclor 1254. Also, Murugesan et al. (2005) illustrated that decreased testosterone levels resulted in weight loss in animals treated with Aroclor 1254.

The significant decrease in total protein, albumin and globulin of rats treated with polychlorinated biphenyls agree with Murugesan et al. (2005) who found that Aroclor 1254 alters the activity of liver metabolic enzymes such as phosphoenolpyruvate carboxykinase and malic acid enzymes involved in protein regulation.

Table 3. The activities of plasma and liver enzymes of male rats treated with quercetin, polychlorinated biphenyls (PCBs) mixture and their combinations

Parameters	Control	Quercetin	PCBs mixture	Quercetin +PCBs mixture
Plasma				
AST (U/L)	36.46±1.120^{b}	37.50±1.811^{b}	49.46±2.586^{a}	40.25±2.135^{b}
ALT (U/L)	24.54±2.239^{b}	23.27±1.316^{b}	31.19±2.216^{a}	25.21±1.193^{b}
AlP (U/L)	68.57±2.885^{b}	66.09±5.556^{b}	84.11±2.451^{a}	72.16±5.701^{ab}
AcP (U/L)	7.43±1.005^{b}	6.38±0.327^{b}	9.62±0.327^{a}	8.08±0.822^{ab}
Liver				
AST (U/mg protein)	76.00±3.047^{a}	74.07±2.390^{a}	65.29±1.932^{b}	62.71±1.778^{b}
ALT (U/mg protein)	39.65±0.538^{a}	38.15±2.551^{ab}	33.94±0.918^{bc}	33.27±1.846^{c}
AcP (U/mg protein)	10.73±0.310^{a}	10.11±0.360^{ab}	9.21±0.341^{b}	8.99±0.457^{b}
AlP (U/mg protein)	72.25±2.413^{a}	70.73±11.289^{a}	63.25±2.124^{a}	60.00±1.046^{a}

Results are demonstrated as means ± SE; n = 8 for each treatment group.
Mean values within a row not sharing a common superscript letters (a, b) were significantly different, p<0.05.
AST = Aspartate aminotransaminase, ALT = Alanin aminotransaminase, ALP = Alkline phosphatase, AcP= Acid Phosphatase.

Table 4. Plasma TBARS, GST activity, GPx activity and SOD activity of male rats treated with quercetin, polychlorinated biphenyls (PCBs) mixture and their combinations.

Parameters	Control	Quercetin	PCBs mixture	Quercetin +PCBs mixture
Plasma				
TBARS (nmol/ml)	0.25±0.036^{b}	0.12±0.005^{c}	0.31±0.015^{a}	0.26±0.005^{ab}
GST (µmol /hr/ml)	1.08±0.122^{ab}	1.27±0.095^{a}	0.86±0.021^{b}	1.03±0.053^{ab}
SOD (U/ml)	1.01±0.064^{ab}	1.14±0.052^{a}	0.74±0.079^{c}	0.84±0.044^{bc}
GPx (U/g wet tissue)	8.18±0.141^{b}	9.09±0.115^{a}	6.19±0.100^{d}	7.14±0.173^{c}
Liver				
TBARS (nmol/g tissue)	42.37±1.769^{a}	33.53±0.480^{b}	43.41±1.203^{a}	42.83±1.787^{a}
GST (µmol/hr/ mg protein)	0.93±0.061^{ab}	1.07±0.050^{a}	0.75±0.063^{c}	0.86±0.066^{bc}
SOD (U/mg protein)	9.08±0.320^{b}	10.86±0.268^{a}	6.19±0.277^{d}	7.68±0.499^{c}
GPx (U/g wet tissue)	31.38±1.523^{b}	37.08±0.898^{a}	21.96±0.416^{d}	27.49±1.202^{c}
Kidney				
TBARS (nmol/g tissue)	21.02±0.340^{bc}	20.02±0.379^{c}	23.28±0.532^{a}	21.52±0.509^{b}
GST (µmol/hr/ mg protein)	0.52±0.049^{ab}	0.62±0.038^{a}	0.39±0.029^{c}	0.45±0.012^{bc}
SOD (U/mg protein)	16.56±0.450^{b}	19.38±0.223^{a}	12.56±0.307^{d}	14.39±0.352^{c}
GPx (U/g wet tissue)	29.61±0.964^{b}	34.53±1.458^{a}	21.77±2.684^{c}	25.21±0.506^{bc}
Brain				
TBARS (nmol/g tissue)	15.81±1.115^{c}	13.49±0.979^{d}	22.10±0.333^{a}	19.44±0.276^{b}
GST (µmol/hr/mg protein)	0.43±0.014^{b}	0.52±0.020^{a}	0.31±0.008^{c}	0.39±0.043^{b}
SOD (U/mg protein)	9.32±0.107^{b}	10.39±0.206^{a}	6.98±0.219^{d}	8.26±0.225^{c}
GPx (U/g wet tissue)	22.35±1.002^{a}	24.63±0.985^{a}	17.78±0.804^{b}	19.76±0.566^{b}
Lung				
TBARS (nmol/g tissue)	19.44±0.852^{b}	15.92±0.709^{c}	21.78±0.361^{a}	20.31±0.490^{ab}
GST (µmol/hr/ mg protein)	0.50±0.034^{b}	0.67±0.024^{a}	0.36±0.028^{c}	0.43±0.007^{bc}
SOD (U/mg protein)	10.93±0.398^{b}	12.61±0.211^{a}	8.42±0.364^{d}	9.37±0.170^{c}
GPx (U/g wet tissue)	24.37±0.749^{b}	28.36±1.092^{a}	19.49±0.990^{c}	21.20±0.503^{c}
Heart				
TBARS (nmol/g tissue)	13.62±0.505^{b}	12.39±0.438^{b}	17.35±1.480^{a}	14.84±1.080^{ab}
GST (µmol/hr/mg protein)	0.74±0.020^{b}	0.83±0.018^{a}	0.60±0.021^{c}	0.68±0.032^{b}
SOD (U/mg protein)	9.86±0.522^{b}	11.14±0.286^{a}	7.76±0.137^{c}	9.09±0.276^{b}
GPx (U/g wet tissue)	22.65±0.853^{b}	25.50±0.932^{a}	18.09±0.937^{c}	20.66±1.137^{b}
Testes				
TBARS (nmol/g tissue)	12.80±0.694^{c}	11.75±0.490^{c}	16.80±0.757^{a}	14.81±0.344^{b}
GST (µmol/hr/ mg protein)	0.53±0.055^{ab}	0.64±0.073^{a}	0.37±0.035^{c}	0.46±0.079^{bc}
SOD (U/mg protein)	16.94±0.389^{b}	18.91±0.264^{a}	13.47±0.262^{d}	14.69±0.196^{c}
GPx (U/g wet tissue)	27.17±0.591^{b}	29.60±0.842^{a}	20.05±0.614^{d}	22.97±0.772^{c}

Results are demonstrated as means ± SE; n = 8 for each treatment group.
Mean values within a row not sharing a common superscript letters (a, b, c, d) were significantly different, p<0.05.
TBARS= Thiobarbituric acid reactive substances, GST= Glutathione S-transferase, GPx= glutathione peroxidase, SOD= Superoxide dismutase.

Table 5. Plasma IgG of male rats treated with quercetin, polychlorinated biphenyls (PCBs) mixture and their combinations.

Parameter	Experimental groups			
	Control	Quercetin	PCBs mixture	Quercetin+ PCBs mixture
IgG (µg/ml)	0.54±0.010^{a}	0.54±0.005^{a}	0.31±0.015^{c}	0.46±0.013^{b}

Values are demonstrated as means ± SE; n =8 for each treatment group.
Mean values within a row not sharing a common superscript letters (a, b, c) were significantly different, p<0.05.

The significant increase in glucose of rats treated with polychlorinated biphenyls mixture are in agreement with Kim *et al.* (2019) who significantly found that Polychlorinated biphenyls (PCBs) have been shown to be associated with diabetes. Plasma glucose is mainly regulated by complex interactions between the liver and the hypothalamus, pituitary gland, and adrenal glands. Therefore, persistent organochlorine compounds can interfere with glucose regulation at multiple checkpoints. They alter the activity of liver metabolic enzymes, such as phosphoenolpyruvate carboxykinase and malic enzyme that are responsible for protein, glucose, and lipid regulation (thereby altering blood concentrations of protein and glucose (Lorenzen *et al.,* 1999).

Quercetin did not affect plasma glucose levels (Table 2), which is consistent with Lügli et al. Match. (2009) who concluded that quercetin; antioxidant flavonoids may regenerate pancreatic islets and increase insulin release in diabetic rats thus has its beneficial anti-diabetic effect.

The significant decrease in bilirubin, the final product of heme degradation, is generally considered a cytotoxic and fat-soluble waste that must be excreted, of rats treated with mixture of polychlorinated biphenyls are in agreement with Arnold *et al.* (1993) who found a decrease in cholesterol and total bilirubin. Sinclair et al. (1997) found that PCBs stimulate the rate of bilirubin degradation. The decrease in urea and creatinine was explained by Chu at al. (2009) who suggested that long-term exposure to PCB mixtures can cause renal dysfunction.

The results of transaminases and phosphatases agree with Kutlu et al. (2007) who found that the exposure to PCBs caused changes in the activities of liver enzymes which is attributed to liver toxicity since the activities of AST, ALT and AlP is proved to be the most sensitive marker used in the diagnosis of hepatotoxicity.

The oxidative stress results agree with Kumar et al. (2004) who found that result of Aroclor 1254 exposure, antioxidant enzyme (SOD) activity and endogenous antioxidant (GSH) levels are reduced, suggesting that the intracellular antioxidant defense system is damaged. The present study found that treatment with quercetin increased GST, SOD and GPx. Also, Rao and Vijayakumar (2007) found that quercetin increased the levels of glutathione, catalase, and superoxide dismutase. Vercelino et al. (2009) reported that quercetin protects cells by inducing antioxidant enzymes.

Lipid peroxidation (LPO) was estimated via evaluating plasma levels of thiobarbituric acid-reactive substances (TBARS), liver, kidney, brain, lung, heart and testes of male rats treated with polychlorinated biphenyls, quercetin and their combinations. The significant increase of plasma TBARS in rats treated with polychlorinated biphenyls mixture agree with Twaroski et al. (2001) who stated that PCB-induced toxic symptoms were proved to be associated with oxidative stress by initiating a self-proliferating LPO response. Significantly increased cytosol concentration of thiobarbituric acid-reactive substances was obtained (Moreira *et al*., 2004).

The significant decrease in plasma TBARS in rats treated with quercetin (Table 4) are in agreement with Bhatt and Flora (2009) who found that quercetin reduced reactive oxygen substances (ROS) in liver and kidney. Papiez et al. (2008) suggested that quercetin may have anti- as well as pro-oxidant role. Also, Wagnera et al. (2006) found that quercetin was able to prevent TBARS formation. Moreover, Rao and Vijayakumar (2007) found that quercetin significantly inhibited the lipid peroxidation.

Results confirmed that treatment with quercetin alone decreased plasma, liver, kidney, brain, lung, heart and testes TBARS. While, treatment with polychlorinated biphenyls mixture alone increased them. The presence of quercetin with polychlorinated biphenyls mixture decreased its toxic effect and decreased the elevated TBARS due to treatment with PCBs mixture.

CONCLUSION

The results of the present investigation convincingly demonstrated that PCBs exposure elevated lipid peroxidation (TBARS), decreased the activities of antioxidant enzymes and IgG and resulted in changes in biochemical parameters in rats. Quercetin is a nutritional supplement that helps in preventing disorders involving PCBs-induced toxic effects on liver, kidney, brain, lung, heart and testes. Quercetin is a powerful antioxidant because of its ability to remove free radicals and to prevent lipid peroxidation reactions. Also, quercetin treatment improved the immunity of rats treated with PCBs mixture and decreased their immunosuppressive effect.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

Arnold, D.L., Bryce, F., Karpinski, K., Mes, J., Fernie, S., Tryphonas, H., Truelove, J., McGuire, P.F., Burns, D., Tanner, J.R., Stapley, R., Zawidzka, Z.Z., Basford, D., 1993. Toxicological consequences of Aroclor 1254 ingestion by female rhesus (macaca mulatta) monkeys. Part 1B. Prebreeding phase: Clinical and analytical laboratory findings. Food Chem. Toxicol., 31(11): 811-824.

Bhatt, K., Flora, S.J.S., 2009. Oral co-administration of α-lipoic acid, quercetin and captopril prevents gallium arsenide toxicity in rats. Environ. Toxicol. Pharmacol., 28(1): 140-146.

Bobadilla, M., Garcia-Sanmartin, J., Martinez, A., 2021. Natural Food Supplements Reduce Oxidative Stress in Primary Neurons and in the Mouse Brain, Suggesting Applications in the Prevention of Neurodegerative Duseases. Antioxidants (Basel.), 10(1): 46.

Bugianesi, R., Serafini, M., Simone, F., Wu, D., Meydani, S., Ferro-Luzzi, A., Azzini, E., Maiani, G., 2000. High-Performance Liquid Chromatography with Coulometric Electrode Array Detector for the Determination of Quercetin Levels in Cells of the Immune System. Analytical Biochem., 284(2): 296-300.

Chu, I., Pelletier, G., Masson, S., Wade, M.J., Nakai, J., Alwis, R., Mohottalage, S., Kumarathasan, P., Black, P., Bowers, W.J., Vincent, R., 2009. Contribution of methylmercury, polychlorinated biphenyls and organochlorine pesticides to the toxicity of a contaminant mixture based on Canadian Arctic population blood profiles. Toxicol. Lett., 184(3): 176-185.

David, A.V.A., Arulmoli, R., Parasuraman, S., 2016. Overviews of Biological Importance of Quercetin: A Bioactive Flavonoid. Pharmcogn. Rev., 10(20): 84-89.

Engvall, E., Perlmann, P., 1971. Enzyme-linked immunosorbent assay (ELISA): quantitative assay of immunoglobulin G. Immunochem., 8: 871.

Engvall, E., 1977. Quantitative enzyme immunoassay (ELISA) in microbiology. Med. Biol., 55: 193.

Habig, W.H., Pabst, M.J., Jakoby, W.B., 1974. Glutathione S-transferases. The first enzymatic step in mercapturic acid formation. J. Biol. Chem., 249: 7130-7139.

IOMC, Inter-Organization Programme for the Sound Management of Chemicals. Geneva, Switzerland: WHO. Persistent Organic Pollutants Assessment Report; 2002.

Kim, Y.A., Park, J.B., Woo, M.S., Lee, S.Y., Kim, H.Y., Yoo, Y.H., 2019. Persistent Organic Pollutant-Mediated Insulin Resistance. Int. Environ. Res. Public Health, 16(3): 448.

Kimbrough, R.D., Jensen, A.A., 2012. Halogenated Biphenyls, Terphenyls, Naphthalenes, Dibenzodioxins and Related Products. Elsevier, 24.

Knerr, S., Schrenk, D., 2006. Carcinogenicity of "non-dioxinlike" polychlorinated biphenyls. Crit. Rev. Toxicol., 36(9): 663-94.

Kumar, J.S., Banudevi, S., Sharmila, M., Murugesan, P., Srinivasan, N., Balasubramanian, K., Aruldhas, M.M., Arunakaran, J., 2004. Effects of Vitamin C and E on PCB (Aroclor 1254) induced oxidative stress, androgen binding protein and lactate in rat Sertoli cells. Reprod. Toxicol., 19(2): 201-208.

Kunz, S., Schwarz, M., Schilling, B., Päpke, O., Lehmler, H.J., Robertson, L.W., Schrenk, D., Schmitz, H.J., 2005. Tumor promoting potency of PCBs 28 and 101 in rat liver. Toxicol. Lett., 164(2): 133-143.

Kutlu, S., Colakoglu, N., Halifeoglu, J., Sandal, S., Seyran, A.D., Aydin, M., Yılmaz, B., 2007. Comparative evaluation of hepatotoxic and Nephrotoxic effects of Aroclor 1221 and 1254 in female rats cell biochemistry and function. Cell Biochem. Funct., 25: 167–172.

Lorenzen, A., Moon, T.W., Kennedy, S.W., Fox, G.A., 1999. Relationships between environmental organochlorine contaminant residues, plasma corticosterone concentrations, and intermediary metabolic enzyme activities in Great Lakes herring gull embryos. Environ. Health Perspect., 107: 179–186.

Lowry, O.H., Rosebrough, N.J., Farr, A.L., Randall, R.J., 1951. Protein measurement with the Folin Phenol Reagent. J. Biol. Chem., 193: 265-275.

Lugli, E., Ferraresi, R., Roat, E., Troiano, L., Pinti, M., Nasi, M., Nemes, E., Bertoncelli, L., Gibellini, L., Salomoni, P., Cooper, E.L., Cossarizza, A., 2009. Quercetin inhibits lymphocyte activation and proliferation without inducing apoptosis in peripheral mononuclear cells. Leukemia Res., 33(1): 140-150.

McCann, M.S., Fernandez, H.R., Flowers, S.A., Maguire-Zeiss, K.A., 2021. Polychlorinated biphenyls induce oxidative stress and metabolic responses in astrocytes. NeuroToxicol., 86: 59-68.

Mishra, H.P., Fridovich, I., 1972. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. J. Biolog. Chem., 247: 3170-3175.

Morales, A..I, Vicente-Sa´nchez, C., Jerkic, M., Santiago, J.M., Sa´nchez-Gonza´lez, P.D., Pe´rez-Barriocanal, F., Lo´pez-Novoa, J.M., 2005. Effect of quercetin on metallothionein, nitric oxide synthases andcyclooxygenase-2 expression on experimental chronic cadmiumnephrotoxicity in rats. Toxicol. Appl. Pharmacol., 210: 128 – 135.

Moreira, A.J., Fraga, C., Alonso, M., Collado, P.S., Zetller, C., Marroni, C., Marroni, N., González-Gallego, J., 2004. Quercetin prevents oxidative stress and NF-κB activation in gastric mucosa of portal hypertensive rats. Biochem. Pharmacol., 68(10): 1939-1946.

Murugesan, P., Senthilkumar, J., Balasubramanian, K., Aruldhas, M.M., Arunakaran, J., 2005. Impact of

polychlorinated biphenyl Aroclor 1254 on testicular antioxidant system in adult rats. Human Exp. Toxicol., 24: 61– 6.

Muthuvel, R., Venkataraman, P., Krishnamoorthy, G., Gunadharini, D.N., Kanagaraj, P., Jone Stanley, A., Srinivasan, N., Balasubramanian, K., Aruldhas, M.M., Arunakaran, J., 2005. Antioxidant effect of ascorbic acid on PCB (Aroclor 1254) induced oxidative stress in hypothalamus of albino rats. Clinica Chimica Acta, 365(1-2): 297-303.

Olayinka, E.T., Ore, A., Echebiri, R.C., 2015. Quercetin, a Flavonoid Antioxidant, Ameliorated Procarbazine-Induced Oxidative Damage to Murine Tissues. Antioxidants (Basel) 2015, 304-321.

Paglia, E., Valentine, N., 1967. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J. Lab. Med., 70: 158-169.

Papiez, M.A., Cierniak, A., Krzysciak, W., Bzowska, M., Taha, H.M., Jozkowicz, A., Piskula, M., 2008. The changes of antioxidant defense system caused by quercetin administration do not lead to DNA damage and apoptosis in the spleen and bone marrow cells of rats. Food Chem. Toxicol., 46(9): 3053-3058.

Rao, C.V., Vijayakumar, M., 2007. Effect of quercetin, flavonoids and α-tocopherol, an antioxidant vitamin on experimental reflux oesophagitis in rats. European J. Pharmacol., 589(1-3): 233-238.

Ross, P., Swart, R.D., Addison, R., Loveren, H.V., Vos, J., Osterhaus, A., 1996. Contaminant-induced immunotoxicity in harbour seals: Wildlife at risk? Toxicol., 112(2): 157-169.

Sinclair, P.R., Gorman, N., Walton, H.S., Sinclair, J.F., Lee, C.A., Rifkind, A.B., 1997. Identification of CYP1A5 as the CYP1A enzyme mainly responsible for uroporphyrinogen oxidation induced by AH receptor ligands in chicken liver and kidney. Drug Metab. Dispos., 25: 779–783.

Tappel, L., Zalkin, H., 1959. Inhibition of lipid peroxidation in mitochondria by vitamin E. Arch. Biochem. Biophys., 80: 333-336.

Twaroski, T.P., O'Brien, M.L., Larmonier, N., Glauert, H.P., Rorbertson, L.W., 2001. Polychlorinated biphenyls-induced effects of metabolic enzymes, AP-1 binding, vitamin E, and oxidative stress in the rat liver. Toxicol. Appl. Pharmacol., 171: 85–93.

Vercelino, R., Tieppo, J., Cuevas, M.J., Tuñon, M.J., Marroni, N.P., Gonzalez-Gallego, J., 2009. Prevention of hepatopulmonary syndrome by quercetin adminstration in cirrhotic rats. J. Hepatol., 50(1): S282.

Venkataraman, P., Krishnamoorthy, G., Vengatesh, G., Srinivasan, N., Aruldhas, M.M., Arunakaran, J., 2008. Protective role of melatonin on PCB (Aroclor 1254) induced oxidative stress and changes in acetylcholine esterase and membrane bound ATPases in cerebellum, cerebral cortex and hippocampus of adult rat brain. Int. J. Dev. Neurosci., 26 (6): 585-591.

Wagnera, C., Fachinettoa, R., Cortea, C.L.D., Britoa, V.B., Severoa, D., Diasb, G.D.O.C., Morelb, A.F., Nogueiraa, C.W., Rochaa, J.B.T., 2006. Quercitrin, a glycoside form of quercetin, prevents lipid peroxidation in vitro. Brain Res., 1107: 192 – 198.

Zeng, Y., Song, J., Zhang, M., Wang, H., Zhang, Y., Suo, H., 2020. Comparison of *In vitro* and *In vivo* Antioxidant Activities of Six Flavonoids with Similar Structures. Antioxidants, 9: 732.