Journal of King Saud University – Science 32 (2020) 1510–1515

Contents lists available at ScienceDirect

Journal of King Saud University – Science

journal homepage: www.sciencedirect.com

Original article

Diosmin protects against acrylamide-induced toxicity in rats: Roles of oxidative stress and inflammation

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ARTICLE INFO

Article history:
Received 15 March 2019
Revised 5 September 2019
Accepted 3 December 2019
Available online 16 December 2019

ABSTRACT

Acrylamide (ACR) is a toxic substance produced by oxidative stress. The recent study focused on stimulation of ACR through ROS intracellular production thereby playing a crucial aspect in the process of toxicity. This is positioned on a relevant research and study on the antioxidant characteristics of diosmin. This research was shown to examine the shielded effect of diosmin against ACR toxicity. Forty rats (male) were grouped in five categories. The control category was given normal saline followed by the second category which was given diosmin (100 mg/kg b.wt oral administered). The next category was given ACR (30 mg/kg b.wt orally) every day for 14 days. The fourth and fifth groups were supplemented by acrylamide (30 mg/kg b.wt) after diosmin given orally (at 50 or 100 mg/kg b.wt for 7days). Upon examination of the specimens over a period of the given time frame, it was found that acrylamide intoxication remarkably rising levels of serum (aspartate transferase, alanine transferase, ALP, urea, creatinine, interleukin 1 beta , and interleukin 6. Besides, it increased the brain, hepatic and renal lipid peroxidation, at the same time, weakening the antioxidant biomarkers accumulation and activities. The introduction of diosmin also alleviated the serum aspartate transferase, alanine transferase, APL, urea, creatinine, as well as plasma pro-inflammatory cytokines such as interleukin-1-beta and interleukin-6. Further to this, both diosmin doses remarkably lowered the levels of MAD in the tissues and nitric oxide which further increased the glutathione, glutathione peroxidase, superoxide dismutase, and catalase, in contrast to the ACR-injected group. Based on these findings, administered diosmin standardized the modified serum framework, halted the peroxidation, and magnified the accumulation and working effects of the biomarker antioxidants in the brain, hepatic and renal tissues of the rats in the current dose-dependent research. Therefore, these findings show that diosmin has a protective reaction in defiance to the toxicity produced by acrylamide through the free radical scavengers along with potent antioxidant occurrences.

1. Introduction

Cooking high-carb foods at extremely elevated temperatures, such as potatoes and grains, facilitates the formation of acrylamide (ACR). ACR is a transparent, inodorous, and crystallized monomer (Tareke et al., 2002), formed by the reaction of glucose with the amino acid asparagine (Becalski et al., 2002). Industries such as textiles, paper, mining, waste water treatment, biotechnology, and cosmetics use the polymerized form of ACR, which is polyacrylamide (Moorman et al., 2012). The absorption of ACR occurs via the process of digestion, respiration, or through the skin (Turkington and Mitchell, 2009) due to reduced molecular weight and upraised water solubility. ACR shifts through the blood/placenta and blood/milk, which are organic membranes (Fuhr et al., 2006). ACR invades the biological particles by synergy of nitrogen of nucleic acids and active vinyl category NH_2 and SH of proteins (Adamsa et al., 2010), resulting into toxicity of neurons, genetics, growth, conception, and malignant growth in human beings and animals (Tareke et al., 2002). ACR is metabolized in 2 ways: via reaction through glutathione to form N-acetyl-S-(3-amino-3-oxypropyl) Cys and N-acetyl-S-(2-carbamoylethyl) Cys or by oxidation to glicidiamine by cytochrome P450 2E1, that demonstrated to be further lethal than ACR (Dybing et al., 2005; Ghanayem et al., 2005). Glycidamide consequently fuses through glutathione or it undergoes chemical breakdown of the components by reacting

Abbreviations: MDA, malondialdehyde; GSH, glutathione; CAT, catalase; CK, creatine kinase; IL, interleukin; ACR, acrylamide.

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

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https://doi.org/10.1016/j.jksus.2019.12.005
1018-3647/

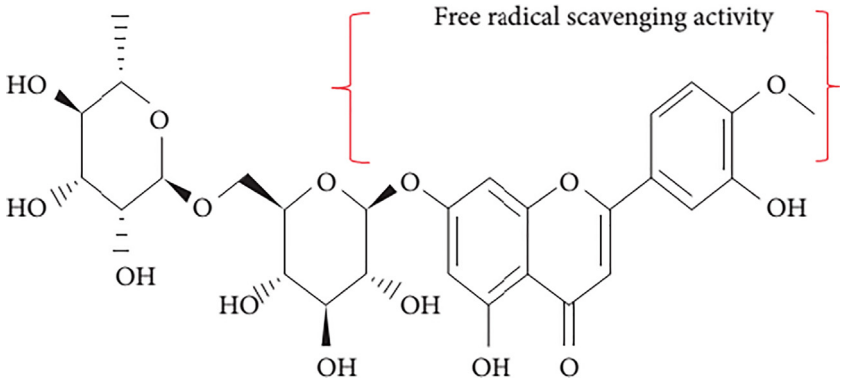

Fig. 1. The chemical structure of diosmin. The area (in brackets) refers to the main antioxidant component of a diosmin molecule.

with water of the epoxide category. It attaches to the proteins of plasma, namely hemoglobin (Xie et al., 2013). ACR toxicity is triggered by oxidative stress. Nevertheless, the protective consequences of exogenous antioxidants that is antagonistic toward oxidative destruction, thereby intercepting the origination of glicidiamine and glycidamide–DNA, adducts (Alturfan et al., 2012). Recent studies promote the pure antioxidant applications due to its mild adverse effects. Diosmin (diosmetin 7-O-rutinoside) is an unsaturated flavonoid glycoside found in citrus fruits (Fig. 1) (Szymański et al., 2016). It is a biologically active polyphenol that possesses anti-inflammatory antioxidant, antihyperglycemic (Srinivasan and Pari, 2012), and antimutagenic properties. Ahmed et al. (2016) demonstrated a nephroprotective role for diosmin against alloxan-induced nephropathy in rat models, while Tahir et al. (2013) highlighted its beneficial effect against alcoholic liver injury. Moreover, diosmin could successfully improve the cardiac functions (Senthamizhselvan et al., 2014) and exert antihyperlipidemic effects against isopropanol-induced myocardial injury in rats (Queenthy, 2013).

Literature survey retrieved no scientific reports on the protective effects of diosmin against ACR toxicity. Therefore, this study aimed to investigate the beneficial role of diosmin versus ACR-induced toxicity in rat liver, renal, and brain tissues based on abovementioned inferences ad through estimation of oxidative stress and proinflammatory biomarkers.

2. Materials and methods

2.1. Chemicals

Pure ACR (99%) and diosmin were purchased from Sigma-Aldrich Chemical Company (St. Louis, Missouri, USA), interleukin (IL)-1β and IL-6 from Glory Science Co. Ltd. (Del TX, USA), and all assay kits from the Biodiagnostics Co. (Cairo, Egypt).

2.2. Animals

Forty Wistar male albino rats weighing approximately 150 ± 25 g were obtained from animal house of King Fahad Medical Research Center. After the acclimatization period, the rats were conserved in a well-aerated room at a temperature of 25 ± 2 °C under 12-h light/dark cycle. Food and water were provided *ad libitum*. The Research Ethical Committee of King Fahad Medical Research Center, Jeddah, KSA approved the rearing and supervising of the animals, including the blueprint of the experiment. All precautions were taken to ensure avoidance of animal stress.

2.3. Experimental design

For the process of adaptation, the rats were kept under surveillance for the conditions listed above for 7 days prior to the experiment. Five different groups with 8 rats each were created: group 1 (control; saline), group 2 (100 mg/kg b.wt diosmin) (Imam et al., 2015), group 3 30 mg/kg b.wt ACR, daily for 14 days) (Tyl et al., 2000), groups 4 and 5 (diosmin 50 and 100 mg/kg b.wt, respectively, for 7 days) (Imam et al., 2015). On day 8, group 4 and 5 rats received 30 mg/kg b.wt ACR daily for 14 days. All doses were orally administered.

2.4. Collection of blood samples and serum with tissue preparation

The blood samples were collected through direct heart perforation. The blood was maintained at a normal room temperature for coagulation, followed by centrifugation for 15 min at 1200*g*. Sera was collected and stored at −20 °C for biochemical analysis. Animals were later decapitated. The, kidney, liver and brain samples of each rat was extricated swiftly and rinsed in saline and placed in an ice cold solution of 50 mmol/L sodium phosphate-buffered saline (100 mmol/L Na_2HPO_4/NaH_2PO_4; pH 7.4) supplemented with 0.1 mmol/L EDTA to eliminate erythrocytes and clots. About 5 ml of ice cold buffer was used for tissue homogenization, and approximately 1 g of the tissue was added to this solution and centrifuged for 30 min at 3000*g*. For further analysis, the obtained supernatant was kept at −80 °C for the examination of antioxidant biomarker and lipid perioxidation.

2.5. Biochemical analysis of serum

The obtained serum was used for colorimetric determination of liver function tests (ALT, AST and ALP) and kidney function tests (urea, and creatinine), using commercial kits purchased from (Biovision Incorporate, USA) according to manufacturer instructions.

2.6. Determination of lipid peroxidation and oxidative stress biomarkers in tissues

Tissues Malondialdehyde TMDA content in kidney, liver and brain tissues was evaluated by lipid peroxidation (Mihara and Uchiyama, 1978). The nitrogen oxide level was directed based on Green et al. (1982). Based on Beutler et al.'s method (1963), Reduced glutathione GSH was determined. Superoxide dismutase SOD, catalase CAT, and glutathione peroxidase GP levels were detected using commercial kits purchased from (Biovision Incorporate, USA).

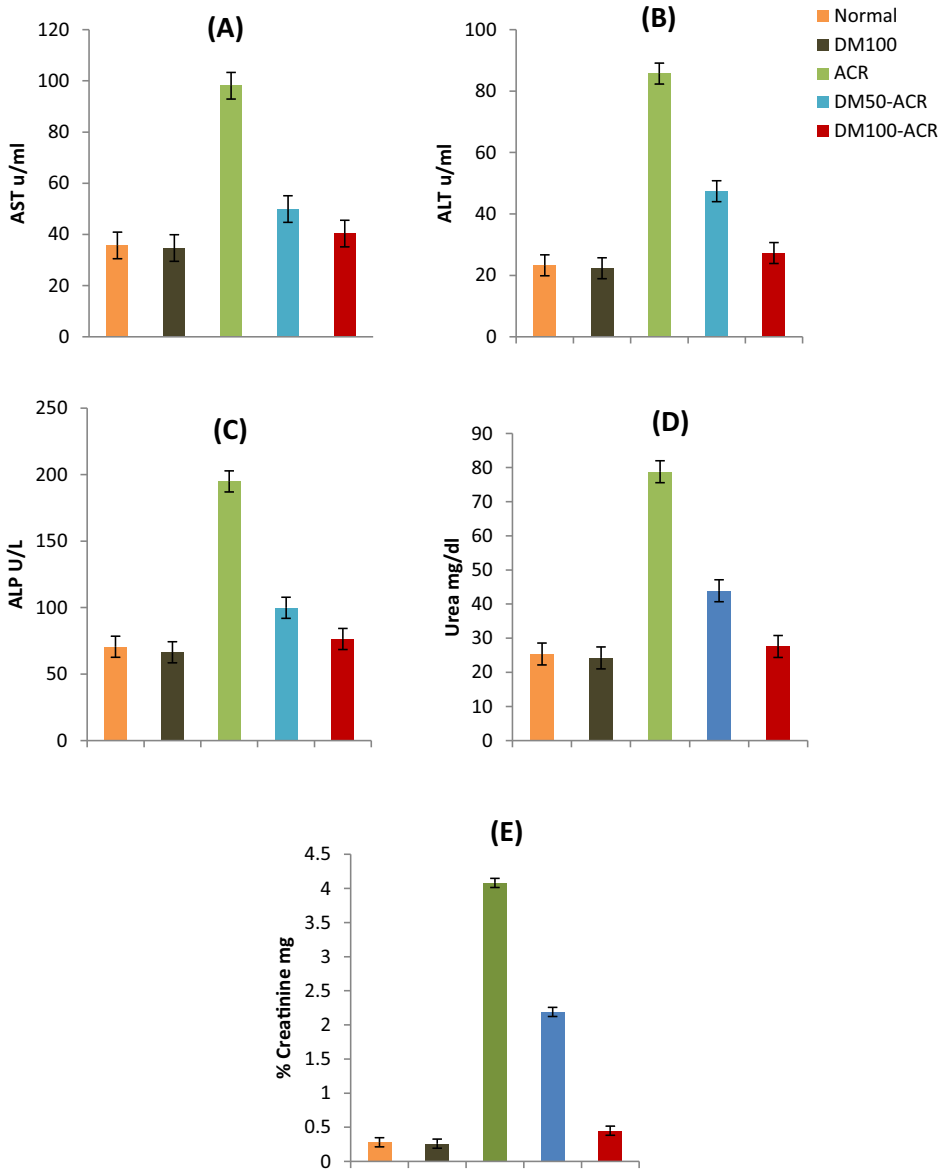

Fig. 2. (A–E). The consequences of diosmin and ACR on the serum level of liver and kidney functions.

Table 1
The consequences of ACR intoxication and administration of diosmin on the peroxidation of lipids and biomarkers activities of the antioxidants of hepatic tissues.

	Groups				
Parameters	Normal	DM100	ACR	DM50-ACR	DM100-ACR
MDA Nmol/g tissue	43.4 ± 2.3	40.4 ± 1.8	82.5 ± 4.6	65.8 ± 4.9	47.9 ± 2.5
NO Nmol/g tissue	62.7 ± 4.8	60.6 ± 5.2	107.4 ± 8.2	77.8 ± 6.2	74.3 ± 5.7
GSH Nmol/g tissue	64.3 ± 4.6	85.4 ± 5.7	30.5 ± 2.1	50.4 ± 3.5	59.4 ± 3.9
GSH-Px Nmol/g tissue	43.7 ± 4.2	58.7 ± 5.6	109.6 ± 7.8	70.3 ± 8.1	67.7 ± 6.7
SOD U/g tissue	19.2 ± 1.1	26.8 ± 2.5	9.1 ± 2.6	14.5 ± 1.6	16.2 ± 1.9
CAT U/g tissue	1.8 ± 0.02	2.3 ± 0.13	0.4 ± 0.04	0.9 ± 0.01	1.4 ± 0.02

Data are expressed as means ± SD. Means within the same row have different superscripts are significantly different at $p < 0.05$.

2.7. Statistical analysis

The statistical analysis was performed using the Statistical Package for Social Science (SPSS program for windows, version 25) (SPSS Inc., Chicago, IL, USA). Data were expressed as mean +/- standard error. The difference between different experimental groups was made using One Way ANOVA (LSD) test. The p value was considered significant when $p < 0.05$.

3. Results

3.1. Biochemical evaluation of serum parameters

Fig. 2(A–E) demonstrates the deteriorating consequences of ACR and the inhibitive consequences of diosmin on the serum biochemical parameters. Rats orally administered with ACR showed remarkably increased ($P \leq 0.05$) levels of liver and kidney function

Table 2
The consequences of ACR intoxication and administration of diosmin on the peroxidation of lipids and biomarkers activities of the antioxidants of the kidney.

Groups	Parameters					
	MDA (nmol/g Tissue)	NO (nmol/mg Tissues)	GSH (mg/g Tissues)	GSH-Px (mol/g Tissues)	SOD (U/g Tissues)	CAT (U/g Tissue)
Control	$78.5^{a} \pm 1.2$	$82.2^{a} \pm 2.2$	$99.4^{a} \pm 3.8$	$44.4^{a} \pm 1.2$	$21.2^{a} \pm 1.1$	$2.1^{a} \pm 0.4$
DM100	$75.3^{a} \pm 1.4$	$79.4^{a} \pm 2.1$	$111.4^{a} \pm 4.2$	$52.8^{a} \pm 1.4$	$26.8^{b} \pm 1.3$	$2.5^{b} \pm 0.9$
ACR	$162.9^{b} \pm 4.7$	$158.3^{b} \pm 5.6$	$48.3^{b} \pm 1.4$	$21.6^{b} \pm 1.1$	$7.3^{c} \pm 0.9$	$0.56^{c} \pm 0.9$
DM50-ACR	$134.3^{c} \pm 3.2$	$126.5^{c} \pm 3.4$	$77.3^{c} \pm 2.1$	$35.2^{c} \pm 1.8$	$15.6^{d} \pm 1.9$	$1.7^{d} \pm 0.8$
DM100-ACR	$79.4^{a} \pm 1.9$	$80.4^{a} \pm 2.2$	$97.2^{a} \pm 3.7$	$43.5^{a} \pm 1.5$	$19.7^{a} \pm 1.7$	$2.0^{a} \pm 0.9$

Data are expressed as means ± SD. Means within the same row have different superscripts are significantly different at $p < 0.05$.

tests, aspartate transferase, alanine transferase, alkaline phosphatase, urea, and creatinine in the serum ($P \leq 0.05$) as compared to control rats. Nevertheless, diosmin administration in ACR-induced rats in groups 4 and 5 changed these parameters significantly in a dose-dependent manner. Diosmin at 50 mg/kg reduced the ($P \leq 0.05$) serum levels in G4 as compared to that in ACR-induced G3. These parameters remained continuously elevated when compared to those in the control group. Diosmin administered at 100 mg/kg in ACR-intoxicated rats in G5 maintained the normal serum levels.

3.2. Lipid peroxidation in the liver and antioxidant system

Table 1 shows the consequences of ACR intoxication and administration of diosmin on the peroxidation of lipids and biomarkers activities of the antioxidants of hepatic. The accumulations of malondialdehyde and nitric oxide in the liver of ACR-induced rats in the G3 showed remarkably elevated ($P \leq 0.05$) levels in contrast to rats in the control rats. Nonetheless, ACR-induction diminished ($P \leq 0.05$) the liver glutathione levels and the functions of glutathione peroxide, superoxide dimutase, and catalase in contrast to those in the control rats. MDA and NO concentration in liver tissues of ACR-induced rats in G3 was notably elevated ($P \leq 0.05$) in contrast to that in control rats. In contrast, rats with ACR-induction showed lower ($P \leq 0.05$) liver glutathione accumulation and glutathione peroxidase, superoxide dismutase, and catalase activities as compared to the control rats. ACR-induced rats in G4 supplemented with 50 mg/kg diosmin showed decreased destructive consequences of ACR on the hepatic accumulations of malondialdehyde, nitric oxide, and glutathione as well as on the functions of glutathione peroxide, superoxide dismutase, and catalase in contrast to those in ACR-induced rats in G3. Nevertheless, the accumulation of these variables was elevated in comparison to that in control rats. The administration of diosmin at the dose of 100 mg/kg inhibited the detrimental consequences of ACR on lipid and antioxidant system on the liver of group 5 rats.

3.3. Lipid peroxidation and antioxidant status of kidney

Table 2 presents the results of kidney antioxidant status involving MDA, NO, and GSH activities in all experimental groups. The ACR induction remarkably increased ($P \leq 0.05$) MDA and NO levels, while a significant reduction ($P \leq 0.05$) was observed in the GSH GSH-Px, SOD, and CAT levels in G3 as compared to that in the control group. Administering the ACR-induced rats with 50 mg/kg diosmin reduced the consequence of ACR on the malondialdehyde, nitric oxide, and glutathione levels and kidney oxidative stress biomarkers in G4 rats. However, they continued to exhibit lower ranges in contrast to those of the control rats. The administration of 100 mg/kg diosmin maintained the malondialdehyde, nitric oxide, and glutathione levels as well as the activities of glutathione peroxide, superoxide dismutase, and catalase in kidney tissues of G5 rats toward the normal levels.

Table 4
The consequences of ACR intoxication and administration of diosmin on the serum ranges of inflammatory cytokines, IL-1, and IL-6.

Groups	Parameters	
	IL-1B (pg/ml)	IL-6 (pg/ml)
Control	$47.8^{a} \pm 3.1$	$48.5^{a} \pm 3.1$
DM100	$45.2^{a} \pm 2.8$	$46.7^{a} \pm 2.6$
ACR	$118.4^{b} \pm 4.3$	$117.4^{b} \pm 4.2$
DM50-ACR	$63.4^{c} \pm 2.5$	$68.3^{c} \pm 1.8$
DM100-ACR	$49.5^{a} \pm 3.7$	$52.1^{a} \pm 1.1$

Data are expressed as means ± SD. Means within the same row have different superscripts are significantly different at $p < 0.05$.

3.4. Brain lipid peroxidation and antioxidant status

Table 3 revealed brain antioxidant status involving the MDA, NO, and GSH activities in all experimental groups. The malondialdehyde and nitric oxide levels were improved ($P \leq 0.05$), whereas the GSH levels and those of glutathione peroxide, superoxide dismutase, and catalase activities were decreased ($P \leq 0.05$) in G3 in contrast control rats. The administration of 50 mg/kg diosmin to ACR-treated rats decreased ($P \leq 0.05$) levels of malondialdehyde and nitric oxide, it increased ($P \leq 0.05$) GSH ranges and glutathione peroxide, superoxide dismutase, and catalase functions in group 4 rats in contrast to that of ACR rats. It is evident that the levels of these parameters are lower than that in the control rats. The

Table 3
The consequences of ACR intoxication and administration of diosmin on the peroxidation of lipids and biomarkers activities of the antioxidants of the brain.

Groups	Parameters					
	MDA (nmol/g Tissue)	NO (nmol/mg Tissues)	GSH (mg/g Tissues)	SOD (U/g Tissues)	GSH-Px (mol/g Tissues)	CAT (U/g Tissue)
Control	$149.8^{a} \pm 3.2$	$151.4^{a} \pm 1.3$	$154.4^{a} \pm 2.3$	$24.6^{a} \pm 1.1$	$73.6^{a} \pm 1.7$	$3.2^{a} \pm 0.85$
DM100	$145.3^{a} \pm 4.1$	$149.1^{a} \pm 2.3$	$160.3^{a} \pm 3.5$	$26.2^{a} \pm 2.1$	$79.9^{a} \pm 1.4$	$3.4^{a} \pm 0.97$
ACR	$313.7^{b} \pm 2.7$	$298.8^{b} \pm 5.4$	$64.8^{b} \pm 1.4$	$7.4^{b} \pm 0.9$	$27.2^{b} \pm 2.1$	$0.9^{b} \pm 0.79$
DM50-ACR	$252.1^{c} \pm 2.2$	$210.7^{c} \pm 3.9$	$99.8^{c} \pm 2.6$	$15.7^{c} \pm 1.5$	$48.5^{c} \pm 3.1$	$2.1^{c} \pm 0.83$
DM100-ACR	$152.9^{a} \pm 1.2$	$172.9^{a,c} \pm 3.4$	$148.4^{a} \pm 2.6$	$21.2^{a} \pm 2.3$	$68.7^{a} \pm 2.5$	$2.5^{d} \pm 0.17$

Data are expressed as means ± SD. Means within the same row have different superscripts are significantly different at $p < 0.05$.

administration of 100 mg/kg diosmin regulated the ranges of these parameters in the affected G5, which was close to the normal control values, albeit showing lower levels.

3.5. Serum inflammatory cytokines

The ACR consequences and the shielding effect of diosmin on the serum ranges of inflammatory cytokines, IL-1, and IL-6 are shown in (Table. 4). The inflammatory cytokines, IL-1, and IL-6 were remarkably elevated ($P \leq 0.05$) in the ACR-induced rats in group 3 as compared to that in control group. Nevertheless, allotting diosmin at a dose of 50 mg/kg in group 4 decreased the serum ranges of the analyzed parameters in contrast to that in group 3. However, their serum ranges remained in compared to normal control rats. The administration of 100 mg/kg diosmin in group 5 brought these parameters to the normal levels.

4. Discussion

The mammalian bodies produce reactive oxygen species (ROS) that are natural metabolism of oxygen (Devasagayam et al., 2004) when neutralized by the endogenous enzymatic and non-enzymatic antioxidant defense system that also includes GST, SOD, and GSH (El-Saleh et al., 2004; Al-Khalaf and Ramadan, 2013). Nevertheless, humans and animals are exposed to ecological contamination as chemicals and xenobiotics that increase the ROS production, thereby creating a disproportion between their generation and neutralization (Al-Khalaf and Ramadan, 2013; Al-Khalaf, 2014). Cell membranes are attacked by ROS, which deteriorate the biomolecules, proteins, lipids, and DNA. Furthermore, diseases such as asthma, atherosclerosis, cancers, and diabetes result from a decrease in the cellular oxidative defense system (Hogg 1998; Al-Khalaf, 2014). Intracellular generation of ROS induced by ACR have a crucial role owing to their toxicity (Zhang et al., 2013). Otherwise, the study highlights—for the first time—the defensive role of diosmin against ACR-induced injuries to the brain, renal, and hepatic tissues of rats. In experimental rats, diosmin could significantly reduce the biochemical alteration induced by ACR. These findings are mostly mediated via the antioxidant and anti-inflammatory effects as shown by the reduction in the levels of oxidative and nitrative stress markers (i.e., MDA and NO), enhanced antioxidant defense mechanisms , and reduced inflammatory cytokines serum levels (i.e., IL-1β and IL-6) after diosmin treatment.

Recent studies affirmed that oral administration of 30 mg/kg b. wt ACR encouraged liver and kidney deterioration, and the inflammatory responses showed elevated serum levels of aspartate transferase, alanine transferase, alkaline phosphatase, urea, creatinine, IL-1, and IL-6 (Fig. 2A–E; Table 4). The data agreed with that of Zhang et al. (2013) who recorded ACR stimulation of hepatic and renal damage and elevated biomarker serum ranges. The elevated ALT, AST, and ALP levels could possibly be the direct result of ACR-induced hepatocyte damage. Furthermore, these damages to liver and kidneys are related to ACR-induced oxidative stress, as ACR induction significantly amplifies the peroxidation of the renal and hepatic tissues along with the brain tissues. The consequence of ACR-induced oxidative stress on the tissues are characterized by increased levels of MDA and NO and functions of the antioxidant enzymes, glutathione peroxidase, superoxide dismutase, and catalase (Tables 1–3). In addition, preceding reports revealed that induction of ACR in animals escalates the lipid peroxidation of kidney and liver tissues (Alturfan et al., 2012; Zhang et al., 2013). Considering that glutathione is a crucial intracellular non-enzymatic antioxidant demonstrating defensive action against varied oxidative stress-induced stimulus, GST makes a fundamental portion of liver toxic by combining them with glutathione, while superoxide dismutase detoxifies superoxide anions. Therefore, glutathione, superoxide dismutase reduce production of ROS (Hayes and Pulford, 1995; Salvemini et al., 2002). Under other conditions, ACR may inhibit the GSH level by binding with glutathione to generate genotoxic, glycidamide, and cancer-causing substances (Pradeep et al., 2007; Klaunig, 2008), thereby contributing to free radicals accumulation, hydroxyl, nitric oxide, and superoxide radicals. Peroxynitrite is produced by the superoxide and NO reaction in occurrence of nitric oxide synthase. The ROS peroxynitrite and hydroxyl radicals are capable of attacking and deteriorating the and biomolecules and cell membranes (Beckman and Koppenol 1996). In addition, inflammatory cytokines can also be activated (Sayed 2008; Alturfan et al. 2012). When ROS generation passes the capacity of – antioxidant defense system to balance their levels, oxidative stress disrupts the cell activities and results in varied conditions that are pathological in nature (Bandyopadhyay et al. 1999). Therefore, our findings indicate that oxidative stress induces renal and hepatic damages by ACR.

With respect to the precautionary effects of diosmin treatment versus ACR–toxicity induction, our results suggest that administration of ACR-induced rats with diosmin results in retained serum levels of brain, hepatic, renal, and inflammatory bio-markers within the normal values. Our results indicate that diosmin treatment can remarkably reduce the serum ranges of inflammatory cytokines IL-6 and IL-1β (Table 4). Consequently, diosmin pre-treatment at either doses could remarkably reduce the serum ALT, AST, and ALP levels and prevented ACR-induced alterations (Fig. 2A–C). These data outcomes agree with those of Tahir et al. (2013), who demonstrated that diosmin decreases the serum transaminases in alcohol-induced hepatic injury. In addition, Tanrikulu et al. (2013) reported an ameliorative efficacy of diosmin on serum transaminases in ischemia/reperfusion-induced liver injury.

In addition, diosmin treatment hindered the peroxidation of lipids along with oxidative stress in the tissues of brain, kidneys, and liver through the elevation of the accumulation of antioxidant functions and enzyme systems (Tables 1–3). Hence, the treatment of diosmin produced a shielding effect against ACR-induced oxidative stress, possibly elaborated by the potential restrictive consequences on peroxidation of lipids and scavenging of free radical due to diosmin inhibition by peroxidation of lipids and elevation of the capacity of the total antioxidant status in the brains, livers, and kidneys. This is due to diosmin, which has a biologically active polyphenol component that possesses anti-inflammatory (Tahir et al., 2013), antioxidant, and antihyperglycemic (Srinivasan and Pari, 2012) properties. The antioxidant action of diosmin has been ascribed to scavenging superoxide anions and hydroxyl radicals (Queenthy and John, 2013). Therefore, by counteracting oxidative stress and rejuvenation of antioxidant defenses, diosmin protect against ACR-induced liver, renal, and brain injury; (ii) the elevated consequences on the molecules of the antioxidants, CAT, SOD, and GSH-Px. Based on our results as well as those of previous reports, diosmin can exert its antioxidant effect directly via free radical scavenging or indirectly by upregulating cellular antioxidant enzymes such as GR, GPx, CAT, and SOD (Arab et al., 2015; Mousa, 2016)

5. Conclusions

AA-induced toxicity is primarily caused by oxidative stress. Diosmin exhibits a dominant antioxidant effect that shields animals from oxidative stress actuated by varied chemicals. This study research revealed that ACR-intoxicated rats with injuries related to the brain, kidney, and liver showed elevated inflammatory

response and lipid peroxidation as well as lowered antioxidant enzyme functions in their tissues. Animal tissues were thus shielded by diosmin from oxidative stress and inhibits destructive consequences of ACR on the antioxidant enzymes organizations, notably at 100 mg/kg dosage. Our research thus suggests that diosmin is a potential protective agent that works against ACR toxicity. As it is widely distributed on citrus fruits the study recommends a daily two citrus fruits to insure a daily constant dose of diosmin.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The author declare that she has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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