Progress in Nutrition 2015; Vol. 17, N.2: 128-136

Original article

Curative effect of orally consumed *Aloe vera* juice on Ochratoxin A-induced nephrotoxicity in rats

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Summary. The current study was designed to evaluate the curative effects of *Aloe Vera* Juice (AVJ) on Ochratoxin (OTA) A-induced nephrotoxicity in rats. AVJ was orally administrated in doses of 150 and 300 mg/kg body weight (BW) for six weeks within gavages daily with OTA (0.5 mg/kg BW) to induce nephrotoxicity. The kidney function markers (uric acid, urea nitrogen, creatinine and albumin), oxidative stress markers (malondialdehyde (MDA)), non-enzymatic (reduced glutathione (GSH), vitamin E) and enzymatic antioxidants (superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidise (GPx)) were determined. In addition, the lipid profile markers such as total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL-C), very low density lipoprotein (VLDL-C) and high density lipoprotein (HDL-C) cholesterols were also estimated. In OTA-induced rats showed significantly increase levels of kidney function markers in serum (uric acid, urea nitrogen, creatinine and albumin), oxidative stress markers in kidney (MDA) and lipid profiles (TC, TG, LDL-C and VLDL-C) in serum except with HDL-C. In addition, the level of non-enzymatic antioxidants (GSH and Vitamin E) and the activities of enzymatic antioxidants (SOD, CAT and GPx) were significantly decreased in OTA-induced rats. Administration of AVJ juice to OTA-induced rats the above biochemical parameters back towards to near normal in control rats. The histological examination of kidney showed more severe degeneration of renal tubules in OTA-induced rats and treatment with AVJ juice showed (300 mg/kg BW) slight hypertrophy of glomerular tuft as well as mild degenerations in renal tubules. In this study, we conclude that the administration of AVJ having beneficial curative effect on OTA-induced nephrotoxicity in rats.

Key words: Aloe vera juice, nephrotoxicity, lipid profile, antioxidants

«Effetto curativo del succo di *Aloe vera* per via orale su ratti con nefrotossicità da Ocratossina A»

Riassunto. Il presente studio è stato progettato per valutare gli effetti curativi del succo di *Aloe vera* (AVJ) su ratti con nefrotossicità da ocratossina A (OTA). AVJ è stato somministrato per via orale in dosi di 150 e 300 mg/kg di peso corporeo (BW) ogni giorno per 6 settimane con OTA (0,5 mg/kg BW) per indurre nefrotossicità. Sono stati valutati i marcatori della funzionalità renale (acido urico, urea, creatinina e albumina), i marcatori dello stress ossidativo (malondialdeide (MDA)), gli antiossidanti non-enzimatici (glutatione ridotto (GSH), vitamina E) e quelli enzimatici (superossido dismutasi (SOD), catalasi (CAT) e glutatione perossidasi (GPx)). Inoltre sono stati valutati gli indicatori del profilo lipidico, come il colesterolo totale (TC), i trigliceridi (TG), il colesterolo-lipoproteine a bassa densità (LDL-C), il colesterolo-lipoproteine a bassissima densità (VLDL-C) e il colesterolo-lipoproteine ad alta densità (HDL-C). Nei ratti OTA-indotti si è evidenziato un aumento significativo dei livelli dei marcatori sierici della funzione renale (acido urico, urea, creatinina e albumina), dei marcatori di stress ossidativo renali (MDA) e dei profili lipidici sierici (TC, TG, LDL-C e VLDL-C) tranne che per HDL-C. Inoltre, il livello degli antiossidanti non enzimatici (GSH e

Vitamina E) e le attività degli antiossidanti enzimatici (SOD, CAT e GPx) erano significativamente diminuiti nei ratti OTA-indotti. La somministrazione di succo AVJ a ratti OTA-indotti ha fatto rientrare nei valori normali dei ratti di controllo, i parametri biochimici citati sopra. L'esame istologico del rene ha mostrato una più grave degenerazione dei tubuli renali in ratti OTA-indotti e il trattamento con succo AVJ (300 mg/kg BW) ha mostrato una lieve ipertrofia del ciuffo glomerulare così come una degenerazione lieve nei tubuli renali. In questo studio, possiamo quindi concludere che la somministrazione di AVJ ha avuto benefici effetti curativi sulla nefrotossicità OTA-indotta nei ratti.

Parole chiave: Succo di Aloe vera, nefrotossicità, profilo lipidico, antiossidanti

Introduction

Ochratoxin A (OTA) is a mycotoxin often found in cereals as a contaminant, and it is known to cause severe nephrotoxicity in animals and humans. It was reported that OTA induces oxidative stress. Lipid peroxidation (LPO) was the first effect observed by diverse authors (1, 2). It is known that oxidative stress may occur in decreased antioxidant defense system or increase in reactive oxygen species (ROS) production (3). The kidney is the main target organ for OTA toxicity. A vast majority of metabolic products of the organism as well as many pharmacological compounds are excreted via the urine.

Medicinal value of plants has been widely investigated for centuries. Many herbs are considered conventional medicines. *Aloe vera* (family Liliaceae), is found predominantly in dry localities in most parts of the world. *Aloe vera* leaves reportedly have tremendous medicinal value. Its juice is commonly used on burns and minor cuts for enhancing healing of dermal wounds (4). It has a long history of use as traditional treatment for its laxative, anti-inflammatory, immunostimulant, antiseptic, wound, burn healing and anti-tumor effects (5-7). Aloe vera gel is approximately 99% water, Chemical components of aloe juice which are responsible for the many putative health benefits, although phenolics such as emodin are largely removed in aloe beverages, polysaccharides remain a major ingredient and these are immunostimulatory (8). This saccharide has been reported to reduce experimental and clinical malignancies and experimental infections when taken orally (9). No detailed investigation has addressed the efficacy of AVJ in treating OTA-induced nephrotoxicity in rats. Thus, the present manuscript addresses the curative effects of AVJ on OTA- induced nephrotoxicity in rats.

Materials and methods

Chemicals

Unless stated otherwise, all chemicals and Biochemical Kits used for determinations were of analytical grade and procured from Sigma Chemicals Co., USA.

Preparation of Aloe Vera Juice (AVJ)

The AVJ juice preparation *(10)*, as followed, Fresh stems of *Aloe vera* were washed thoroughly to get rid of all forms of debris. The leaves were then sliced longitudinally to cut open the inner part of the leaves. The gel in the leaves was scrapped into a beaker and blended to obtain a finer and liquefied form of the gel, the aloe juice. The juice was refrigerated below 4 °C for preservation.

Preparation of basal diet

The basal diet was prepared using AIN-93(11), It consists of 20% protein (casein), 10% sucrose, 4.7% corn oil, 2% choline chloride, 1% vitamin mixture, 3.5% salt mixture and 5% fibers. The remainder was corn starch up to 100%.

Experimental animals

Fifty adult male rats of Sprague Dawley Strain weighing 220 ± 20 mg were procured from the college of pharmacy, King Saud University, KSA and they were maintained in an air conditioned room (25 ± 1 ˚C) with a 12 h light/12 h dark cycle. Feed and water were provided *ad libitum* for one week before the start of experiment for adaptation. Procedures involving animals and their care were approved by the CAMS Research Ethics Committee, King Saud University.

Experimental design and induction of nephrotoxicity

After acclimatization, rats were randomly divided into five groups, each contains eight rats feed on basal diet. Group 1 (normal control) none treated. Group 2 gavaged daily AVJ with 300 mg/Kg body weight (as maximum dose). Group 3 was served as OTA treated group (positive control), was gavaged daily with OTA (0.5 mg/kg BW) to induce nephrotoxicity (12). Group 4 and 5 were given AVJ at the doses of (150 mg/kg and 300 mg/kg BW) respectively. All these treatments were given orally daily for 6 weeks. Feed intake was calculated daily and the body weight gain was recorded weekly (13). Feed efficiency ratio (FER): FER = weight gain (g)/ feed intake (g) was then calculated. At the end of experimental period, the animals were anesthetized by anesthetic ether and the blood was collected. The kidneys were immediately dissected out, washed in ice-cold saline to remove the blood. Tissues were sliced into pieces and homogenized in an appropriate buffer (pH 7.0) in cold condition to give 20% homogenate (w/v). The homogenates were centrifuged at 1000 rpm for 10 min at 0˚C in cold centrifuge. The supernatants were separated and used for various biochemical estimations.

Assessment of nephroprotective activity

The collected blood was allowed to clot and serum was separated at 2500 rpm for 15 min and the biochemical parameters like serum enzymes: aspartate aminotransferase (AST, U/L), alanine aminotransferase (ALT, U/L)(14), alkaline phosphatase (ALP, U/L) (15), Serum cholesterol was determined according to the enzymatic method described by Allain et al.(16) serum triglycerides were colorimetrically determined according to Wahlefeld,(17) the HDL-c was determined according to Albers et al.(18), while concentration of VLDL-c was estimated according to the Friedewald's equation(19). Low density lipoprotein cholesterol can be calculated as follows:

LDL-c = Total cholesterol – (HDL-c) – (VLDL-c)(19).

Serum urea nitrogen, uric acid and creatinine were determined according to the methods described (20-22). Albumin in the serum was estimated by Biuret method (23).

Lipid peroxidation and non-enzymatic antioxidants biomarkers:

Kidney homogenates were used for the determination of tissue lipid peroxide (MDA), non enzymatic antioxidants biomarkers (GSH and Vitamin E) and enzymatic antioxidants biomarkers (SOD, CAT and GPx).

Kidney homogenates were used for determination of tissue lipid peroxide (MDA), non-enzymatic antioxidant biomarkers (GSH), and enzymatic antioxidant biomarkers (SOD and CAT). Lipid peroxidation (LPO) was determined by quantifying malondialdehyde (MDA) that formed in terms of thiobarbituric acid reactive substances (TBARS) (24). As follows: In a centrifuge tube, 600 µl of trichloroacetic acid solution (10%, w/v) were added to 300 µl of the kidney slices homogenate and centrifuged at 10,000 rpm for 10 min; 400 µl of supernatant were taken in a clean test tube then mixed well with 400 µl of thiobarbituric acid solution (0.67%, w/v). After 30 min in a boiling water bath, the reaction mixture was cooled to room temperature, and the absorbance (A) was measured at 532 nm using a Jenway 6300 spectrophotometer. The malondialdehyde (MDA) content (µmol/ml) was calculated using molar extinction coefficient (156,000 M/cm). The data are expressed as MDA equivalents (µmol/mg protein). The levels of vitamin E were determined as method used by Baker et al.(25) Reduced glutathione (GSH) was estimated using the methods of Ellman, (26) as follows; 0.1 ml of kidney tissue homogenate, 2.4 ml of 0.02M EDTA solution was added and kept on an ice bath for 10 min. Then 2 ml of distilled water

and 0.5 ml of 50 % TCA were added. This mixture was kept on ice for 10-15 min and then centrifuged at 3000 rpm for 15 min; 1 ml of supernatant was taken and 2 ml of Tris-Hcl buffer was added. Then, 0.05 ml of DTNB solution (Ellman's reagent) was added, followed by thorough vortexing. OD was read (within 2-3min after addition of DTNB) at 412 nm against a reagent blank. Absorbance values were compared using a standard curve generated from known GSH.

Enzymatic antioxidant biomarkers

The activities of kidney tissue superoxide dismutase (SOD) was determined calorimetrically (27), in brief, for SOD activity assays, kidney tissue was homogenized in 50 mM potassium phosphate buffer, pH 7.8, and SOD activity in the homogenates was measured using the nitroblue tetrazolium (NBT)-bathocuproine sulfonate (BCS) reduction inhibition method. Sodium cyanide at 5 mM was used to inhibit Cu/ZnSOD and thus measure only MnSOD activity. BCS and sodium cyanide were purchased from Aldrich. Catalase (CAT) was determined using, the Sinha method (28), based on reduction of dichromate in acetic acid to chromic acetate when heated in the presence of hydrogen peroxide, chromic acetate was measured at 570 nm. One unit of CAT activity is defined as the amount of enzyme that degrades one mmol H2O2/min. Glutathione peroxidase (GPx) were determined with minor modification(29) as a unit of glutathione peroxidase activity is taken as the amount of enzyme which consumes 1/ µmol NADPH/min.

Histopathological studies

Small pieces of kidney tissues fixed with 10% phosphate buffered neutral formalin, dehydrated in graded (50-100%) alcohol and embedded in paraffin. Sections (5 mm) were stained with routine hematoxylin and eosin, examined for histopathological studies.

Statistical analysis

Data were analyzed by one-way analysis of variance followed by Duncan's Multiple Range Test (DMRT) using SPSS version 11 (SPSS, Chicago, IL). The limit of statistical significance was set at $P<0.05$.

Table 1. Effect of AVJ doses on body weight gain feed intake and feed efficiency ratio (FER) against OTA-induced nephrotoxicity in rats.

Groups Parameters	Normal Control	Normal + max dose (300 mg/kg)	Positive Control	AVJ (150 mg/kg)	AVJ (300 mg/kg)
Weight gain (g)	17.48	18.37	15.12	17.75	17.89
Feed intake (g/day)	37.23±0.89 b	37.23±1.54 b	26.56±2.13 c	38.31±1.07 b	40.42±1.79 a
FER	0.088±0.002 b	0.093±0.004 a	0.077±0.001 c	0,091±0.002 a	0.092±0.007 a

Values are means ± S.D n= 8 rats/group.
Values not sharing a common superscript differ significantly at p< 0.05 (DMRT).

Table 2. Effect of AVJ doses on serum lipid profiles against OTA-induced nephrotoxicity in rats.

Groups Parameters	Normal Control	Normal + max dose (300mg/kg)	Positive Control	AVJ (150 mg/kg)	AVJ (300 mg/kg)
TC (mg/dl)	66.84±4.12 cd	67.41±3.4 cd	146.91±5.12 a	82.94±4.5 b	68.52±4.79 c
TG (mg/dl)	61.08±4.8 d	61.96±3.9 d	110.38±2.3 a	73.46±3.96 bc	65.72±3.6 cd
HDL (mg/dl)	49.19±2.5 a	51.02±2.9 a	32.84±1.6 c	38.48±3.5 bc	45.37±3.6 a
LDL (mg/dl)	16.26±1.98 d	18.13±1.96 d	74.92±1.89 a	25.41±1.85 bc	15.47±1.86 cd
VLDL (mg/dl)	13.37±0.96 c	12.39±0.78 c	22.07±0.46 a	14.69±0.79 c	13.14±0.72 c

Values are means ± S.D n= 8 rats/group.
Values not sharing a common superscript differ significantly at p< 0.05 (DMRT).

Results

It was observed that administration different levels of AVJ (150 and 300 mg/ kg body weight) was showed a significant increase in feed intake and food efficiency ratio (FER) compared to nephrotoxicity control rats. No significant differences in feed intake and FER were observed between AVJ groups. In context, (normal + max dose) group showed no significant increase in feed intake and FER compared to normal control rats.

Table 2 shows the effect of AVJ on serum lipid profiles of normal control and OTA-induced nephrotoxicity in rats. Administration of OTA (0.5 mg/kg body weight) resulted in a significant ($p<0.05$) increase in total cholesterol, triglycerides, low density lipoprotein (LDL-c), and very low density lipoprotein (VLDL-c) while the level of high density lipoprotein (HDL-c) showed a significant ($p<0.05$) decrease compared with normal control. Treatment with AVJ (150 and 300 mg/ kg BW) resulted in significant ($p<0.05$) changes of lipid parameters towards normal levels. In addition normal rats feed AVJ with max dose (300 mg/kg body weight) resulted in non significant increase in all lipid profile compared to normal control vise versa very low density lipoprotein (VLDL-c).

Tables 3 and 4 show the effect of AVJ on serum kidney function markers of normal control and OTA-induced nephrotoxicity rats. OTA-induced rats showed a significant ($p<0.05$) increase in serum hepatic biomarkers AST, ALT, and ALP compared with normal control. In addition, serum uric acid, urea nitrogen, creatinine and albumin showed a significant ($p<0.05$) increase in induced control compared with normal control. Administrated of AVJ to OTA-induced rats the liver and kidney function markers were significantly ($p<0.05$) decreased when compared to OTA-induced rats. In addition, the normal group treated with max dose (300 mg) showed no significant ($p<0.05$) decrease in liver and kidney function markers compared to normal control feed in basal diet.

The effect of AVJ administration with different levels on rat kidney lipid peroxidation, vitamin E and glutathione levels of OTA-induced nephrotoxicity in rats are shown in the Table 5. The levels of lipid peroxidation were significantly ($p<0.05$) increased in rats treated with OTA as compared to the normal control. Administration with AVJ levels (150 and 300 mg) caused a significant ($p<0.05$) decrease in levels of lipid peroxidation and brought them near to normal level especially for group (OTA + 300 mg). A significant

Table 3. Effect of AVJ doses on serum AST, ALT and ALP against OTA-induced nephrotoxicity in rats.

Groups Parameters	Normal Control	Normal + max dose (300 mg/kg)	Positive Control	AVJ (150 mg/kg)	AVJ (300 mg/kg)
AST (U/dl)	72.22±4.2 c	70.30±3.8 c	109.26±5.2 a	93.08±3.7 b	81.66±3.5 c
ALT (U/dl)	39.27±2.7 c	38.03±2.8 c	90.31±4.6 a	72.67±3.5 b	58.81±3.2 c
ALP (U/dl)	36.21±2.1 c	36.01±1.9 c	87.77±1.7 a	49.68±3.1 b	41.52±2.9 bc

Values are means ± S.D n= 8 rats/group.
Values not sharing a common superscript differ significantly at p< 0.05 (DMRT).

Table 4. Effect of AVJ doses on serum kidney functions and albumin against OTA-induced nephrotoxicity in rats.

Groups Parameters	Normal Control	Normal + max dose (300mg/kg)	Positive Control	AVJ (150 mg/kg)	AVJ (300 mg/kg)
Urea nitrogen (mg/dl)	32.80±2.32 bc	32.14±2.13 bc	61.71±2.59 a	38.47±6.11 b	33.42±5.11 bc
Uric acid (mg/dl)	1.22±0.13 bc	1.19±0.12 bc	2.31±0.18 a	1.71±0.13 b	1.44±0.16 b
Creatinine (mg/dl)	1.10±0.02 bc	1.09±0.02 bc	1.65±0.04 a	1.40±0.03 b	1.20±0.01 bc
Albumin (mg/dl)	3.92±0.26 a	3.82±0.29 a	2.66±0.43 c	2.93±0.34 b	3.37±0.31 ab

Values are means ± S.D n= 8 rats/group.
Values not sharing a common superscript differ significantly at p< 0.05 (DMRT).

Table 5. Effect of AVJ doses on kidney tissues Lipid peroxidation and non-enzymatic antioxidants against OTA-induced nephrotoxicity in rats.

Groups Parameters	Normal Control	Normal + max dose (300 mg/kg)	Positive Control	AVJ (150 mg/kg)	AVJ (300 mg/kg)
MDA (nmol/min/mg protein)	0.12±0.03 bc	0.12±0.02 bc	0.31±0.04 a	0.20±0.03 ab	0.16±0.02 b
Vitamin E (mmol/100 g wet tissue)	3.08±0.29 a	2.93±0.35 a	1.32±0.19 c	2.20±0.21 b	2.69±0.32 a
GSH (nmol/min/mg protein)	14.82±1.37 a	15.91±1.12 a	8.89±0.87 c	11.71±0.89 b	12.56±1.10 ab

Values are means ± S.D n= 8 rats/group.
Values not sharing a common superscript differ significantly at p< 0.05 (DMRT).

Table 6. Effect of AVJ doses on the activity of antioxidant enzymes in kidney tissues against OTA-induced nephrotoxicity in rats.

Groups Parameters	Normal Control	Normal + max dose (300 mg/kg)	Positive Control	AVJ (150 mg/kg)	AVJ (300 mg/kg)
SOD (U/mg protein)	18.59±1.01 a	19.21±1.03 a	8.73±0.83 c	12.13±0.86 b	16.64±0.70 ab
CAT (nmol/min/mg protein)	41.13±2.30 a	43.98±2.49 a	20.96±1.87 c	28.95±2.05 bc	36.40±2.34 b
GPx (nmol/min/mg protein)	11.09±0.51 a	11.21±0.47 a	5.05±0.34 c	7.18±0.58 bc	9.02±0.50 b

Values are means ± S.D n= 8 rats/group.
Values not sharing a common superscript differ significantly at p< 0.05 (DMRT).

($p<0.05$) decrease in levels of vitamin E and GSH, were noted after administration of OTA. When rats were gavaged AVJ, the levels of vitamin E and GSH were significantly ($p<0.05$) changed to near normal.

Table 6 reveals the activities of enzymatic antioxidants such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) in kidney tissues of normal and OTA-induced nephrotoxicity in rats. The results showed that the significant changes were observed the activity of enzymatic antioxidants in kidney against OTA-induced nephrotoxicity in rats. OTA produced a significant ($p<0.05$) decrease of SOD, CAT and GPx enzymes activities in kidney when compared to normal control. Rats gavaged with AVJ the activities of enzymatic antioxidants such as SOD, CAT and GPx were significantly ($p<0.05$) increased when compared to normal control rats. However, the normal rats treated with maximum dose of AVJ was showed no significant ($p<0.05$) increase in enzymic antioxidants when compared to normal control.

Microscopic examination of normal control group, showed the normal histological structure or renal parenchyma (Fig. 1a). The kidney of OTA-induced rats showed more severe degeneration alteration, vacu-

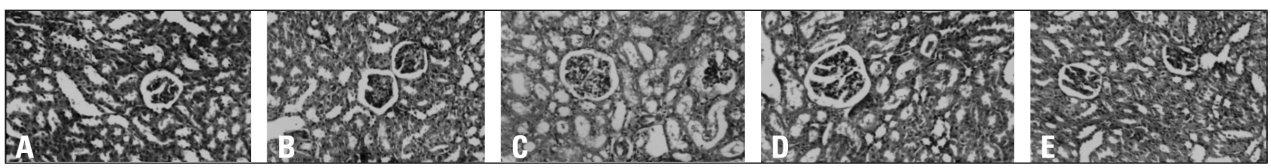

Figure 1. Effect of Aloe Vera Juice (AVJ) by different doses on histological kidney examinations of OTA-induced nephrotoxicity in rats. Photo A): Kidneys of rat from groups 1 (normal control) showing the normal histopathological structure of renal parenchyma (H and EX 200); Photo B): Kidneys of rat from groups 2 (normal+max dose) showing the normal histopathological structure of renal parenchyma (H and EX 200); Photo C): Kidneys of rat from group 3 (induced control) showing vacular degeneration of epithelial lining glomerular tufts as well as epithelial lining renal tubules (H and EX 200); Photo D): Kidneys of rat from group 4 (AVJ 150mg) showing slight hypertrophy of glomerular tuft as well as presence of eosinophilic protein cast in the lumen of some renal tubules (H and EX 200); Photo E): Kidneys of rat from group 5 (AVJ 300mg) showing apparent normal renal parenchyma (H and EX 200).

olar degeneration of endothelial lining glomerular tufts and epithelial lining renal tubules (Fig. 1c). In addition, microscopic examination of kidney tissues of rats administrated AVJ (150 mg/kg body weight) showed congestion of glomerular tufts and granularity of epithelial lining renal tubules (Fig. 1d), while microscopic examination of kidneys for AVJ (300 mg/kg body weight) group showed slight hypertrophy of glomerular tuft as well as mild presence of eosinophilic protein cast in the lumen of some renal tubules (Fig. 1e). In same context, histological structure of kidney tissues of normal + max dose of AVJ rats showed apparent normal histological structure (Fig. 1b).

Discussion

More attention has been paid to the protective effects of natural antioxidants against drug-induced toxicity (30). A recent report has shown that the organic extracts of *Aloe Vera* leaf possess potent *in vivo* antioxidant capacity (31). The organic extract of *Aloe Vera* leaves provided anti-inflammatory activity in the experimental rats (32). *Aloe vera* has also been shown to be a potential therapeutic agent for the treatment of sepsis and hepatotoxicity (33,34). Therefore, current study, we planned to investigate the Curative effects of orally consumed *Aloe vera* L. juice on Ochratoxin A-induced nephrotoxicity in albino rats.

The decreased level of body weight may explained by the ability of OTA to generate free radicals, which may lead to DNA breakage, inhibition of protein biosynthesis and gluconeogenesis, lipid peroxidation (35). Ample evidence exists with respect to the fact that HDL cholesterol is inversely related to total body cholesterol and a reduction of plasma HDL cholesterol concentration may accelerate the development of atherosclerosis leading to ischemic heart disease, by impairing the clearing of cholesterol from the arterial wall (36,6). Administration of AVJ to OTA-induced rats the decreased levels of body weight, FER, HDL-C and increased levels of TC, TG, LDL-C, and VLDL-C were back towards to normal control rats. Antioxidant contents found in AVJ could therefore be considered favorable in increasing HDL and decreasing TC, TG, LDL, and VLDL in AVJ treated groups (37).

The liver enzymes, alanine-aminotransferase (ALT) and aspartate-aminotransferase (AST) are used routinely for assessing liver function. ALT, produced mainly in the liver catalyzes the transfer of amino groups between L-alanine and glutarate to meet physiological needs. AST is found in many body tissues including the heart, muscle, kidney brain, and lung. It is also present in the liver. AST catalyzes the transfer of amino and keto groups between alpha-amino acids and alpha-keto acids thereby acquiring the term transferase. Increased activities of AST, ALT and ALP were observed in OTA-induced rats, which are due to granular and vacuolated degeneration cell necrosis resulted in leakage of these enzymes from the cytosol into the blood stream (38). Administration of AVJ to OTA-induced rats the activities of AST, ALT and ALP were significantly ($p< 0.05$) attenuated that may be due to AVJ to protect against pro-oxidant-induced membrane and hepatic cellular damage, through enhancing microsomal and cytosolic protein, in addition protein synthesis (39).

The OTA may be directly linked to kidney diseases and possibly carcinogenicity (40) therefore, the increased levels of kidney function markers were observed clearly in OTA-induced group. Concerning kidney functions, rats treated with OTA was showed a significant ($p< 0.05$) increase in uric acid, urea nitrogen, creatinine and in albumin levels. The elevated urea level in nephrotoxic rats is likely due to increased amino acid catabolism, impaired kidney function (2, 38). Creatinine is thought to be a more reliable indicator of kidney function as it shows how well the kidneys are filtering out toxins and is less dependent on dietary factors and hydration status. When rats gavaged orally different levels of AVJ, the increased levels of serum kidney function markers were significantly ($p< 0.05$) attenuated to near normal rats, which may be due to minimized OTA toxicity, which might be associated with disorders in intra renal prostaglandins and abnormalities in the renal nitric oxide system induced by lipid peroxidation or its effect on renal cells based on the oxidative stress action and enhancing renal functions.

Oxidative stress induces the production of highly reactive oxygen species that are toxic to the cell, particularly the cell membrane in which these radicals interact with the lipid bilayer and produce lipid peroxides. However, endogenous antioxidant enzymes (superoxide

dismutase, catalase, and glutathione peroxidase) are responsible for the detoxification of the deleterious oxygen species (40). The OTA is associated with ROS production, when there is reduction or depletion in endogenous antioxidants defenses contents, macromolecules become a target for oxidative generations of reactive species (41). In agreement with other studies (8, 38, 42). we observed a significant ($p< 0.05$) increase in the levels of lipid peroxidative markers in kidney tissues malondialdehyde (MDA) of OTA-induced rats to more than 1.5-fold of the results observed in normal control, and administration of AVJ to OTA-induced rats significantly decreased the level of these MDA. In addition, the levels of non-enzymatic antioxidants such as vitamin E, GSH and the activities of enzymatic antioxidants such as SOD, CAT and GPx were decreased significantly ($p< 0.05$) in OTA-induced rats. The administration of AVJ to OTA-induced rats were shown that the above parameters; lipid peroxidation, enzymatic and non-enzymatic significant ($p< 0.05$) restored to near normal control rats. These observations demonstrate the antiperoxidative and antioxidant effects of AVJ. Results were in agreement with others reported (43-44).

The conclusion, results of this study have demonstrated that the AVJ can ameliorate the development of oxidative stress and to protect against OTA- induced nephrotoxicity. In addition, the administration of AVJ can attenuate the abnormalities of lipid profiles, liver and kidney biomarkers. The marked increase in the nephroprotective effect with restoring the antioxidant enzyme concentrations to near the normal levels appeares in decreasing the level of MDA and increasing the vitamin E, GSH, SOD, CAT and GPx status, may be due to AVJ antioxidant properties that help to enhance the detoxification reaction of the cell. In addition, the histological observation for kidney tissues supports those findings.

Acknowledgements

The authors would like to extend their sincere appreciation to the Deanship of Scientific Research at King Saudi University for its funding of this research through the research group project no (RGP-193).

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