

Antioxidant Activity of Some Agro-Industrial Peels on Liver and Kidney of Rats Exposed to Oxidative Stress

M.A. Abd El-Ghany, M.A. Ramadan and S.M.M. Hassanain

Department of Home Economics, Faculty of Specific Education, Mansoura University, Egypt

Abstract: Forty-nine adult albino male rats Sprague -Dawley strain were randomly classified into six groups (7 rats each). The first group served as a normal control group, fed on standard diet only. The other five groups were fed on standard diet and received 0.4 g/l of potassium bromate and 0.5 g/l cadmium chloride in drinking water and 5g/ kg body weight/24h of ethanol in diet for four weeks to induce oxidative stress in liver and kidney. Then, rats reclassified into 5 groups which were positive control (untreated) and treated rat groups that were mango, apple, potato and mixture peels groups. The treatment period is designed for four weeks. The results revealed that, positive control group showed only a significant increase in food efficiency ratio, serum alanine and aspartate amino transferase (ALT & AST), alkaline phosphatase (ALP) enzymes activity, albumin/globulin ratio (A/G), uric acid, creatinine, urea, malondialdehyde (MDA), cholesterol, triglyceride, low density lipoprotein cholesterol (LDLc), very low density lipoprotein cholesterol (VLDLc) and cholesterol/high density lipoprotein cholesterol (HDLc) but a significant decrease in packed cell volume (PCV), white blood cells (WBCs), hemoglobin (Hg) and red blood cells (RBCs), total protein (TP), globulin, superoxide dismutase (SOD), glutathione peroxidase (GSP), catalase, HDLc in comparing with normal control group. Mango group showed a significant decrease in weight gain %, Hg, PCV, SOD and GSP but showed a significant increase in albumin, MDA, cholesterol and LDLc, while apple group showed a significant decrease in final weight, FER, weight gain, weight gain (%), Hg, PCV, A/G ratio, SOD, catalase and GSP but a significant increase in cholesterol, LDLc and MDA in comparing with normal control group. Potato group showed a significant decrease in weight gain (%), A/G ratio, Hg, PCV, urea, SOD, catalase and GSP but significant increase in globulin and MDA, while mixture group showed a significant decrease in final weight, weight gain, weight gain percent, A/G ratio, triglyceride, SOD, catalase and GSP but a significant increase in globulin and MDA in comparing with normal control group. Histopathological results revealed improvement in liver and kidney histology in all groups which treated with mango, apple, potato and mixture peels.

Key words: Oxidative stress • Mango • Apple and potato peels

INTRODUCTION

A human and animal exposure is usually exposed concurrently or sequentially to multiple environmental chemicals from a variety of sources, including drinking water. Public drinking water treated with chemical disinfectants contains a complex mixture of disinfection by-products for which the relative toxicity of the mixtures needs to be characterized to accurately assess risk. Toxicities associated with the transition metals could be due to oxidative tissue damage as they catalyze oxidative reactions in biological macromolecules [1]. Potassium bromate (KBrO₃), cadmium chloride and ethanol are at a

concentration equal to World Health Organization maximum permissible limit can cause oxidative stress. Potassium bromate is a by-product from ozonation of high-bromide surface water for production of drinking water and is also a flour improver that acts as a maturing agent. It is a food additive for the past as it acts principally in the late dough stage giving strength to the dough during the late proofing and early baking [2]. The mechanism of potassium bromate induced toxicity has focused on oxidative stress as a key event in the induction of these carcinomas. It is a rodent carcinogen that produces thyroid, mesothelial and renal tumors [3].

Cadmium is a heavy metal of high toxicity and is present in the environment and one of the most toxic metals to biological systems including marine organisms and its toxicity includes the interference in various metabolic processes, especially energy metabolism, membrane transport and protein synthesis and may act on DNA directly or indirectly by interference with genetic control and repair mechanisms. Furthermore, cadmium can compete with essential metals in protein-binding sites leading to the release of Fe^{2+} and Cu^{2+} ions causing increased production of reactive oxygen species and oxidative stress [4]. Prolonged consumption of ethanol also increases the production of reactive oxygen species, in particular through the activation of cytochrome in the well known microsomal ethanol oxidation system [5]. Ethanol can influence turnover and modify some effects of its action, including nephro- and hepatotoxicity as well as disturbances in the metabolism of bioelements such as zinc, copper and iron. The interactions between cadmium and ethanol can influence the oxidative status of the organism and in this way modify the risk of health damage in cadmium exposed alcoholics [6]. Imbalance production and consumption of reactive oxygen species, leading to oxidative stress, is implicated in the pathophysiology of a plethora of genetic and acquired disorders, such as cancer, arteriosclerosis, malaria and rheumatoid arthritis, as well as neurodegenerative diseases and ageing process [7].

Agro-industrial by-products are good sources of phenolic compounds and have been explored as source of natural antioxidants. While the use of naturally occurring phenolic compounds as food antioxidants is particularly interesting. Phenolic compounds profile of these by-products has to be resolved to obtain the optimum antioxidant efficiency. The peel and seed fractions of some fruits possess higher antioxidant activity than the pulp fractions [8]. The present study was undertaken to evaluate the utilization of mango, apple and potato peels as natural antioxidants to prevent the side effect of free radical in the experimental rats.

MATERIALS AND METHODS

Materials

Mango Peels and Apple Peels: Fresh mango (*Mangifera indica* L., Anacardiaceae) and apple peels (*Golden Delicious* sp., Rosaceae) were obtained from Best Factory for soft drink in El-Dakahlia Governorate, Egypt at the end of July and May 2009, respectively, while fresh potato peels were obtained from local restaurant in El-Dakahlia Governorate, Egypt at the end of December 2009.

Chemicals: BioMeriueX Kits were purchased from Alkan Co. for Chemicals and Biodiagnostics, Dokki, Egypt. Potassium bromate ($KBrO_3$) and cadmium chloride both are white crystalline powder purchased from El-Gomhoria Company, El-Mansoura city, Egypt. Ethanol (CH_3CH_2OH) is colorless liquid with a characteristic agreeable odour, obtained from El-Gomhoria Company, El-Mansoura City, Egypt. Standard diet was prepared according to NRC [9].

Animals: Forty two Sprague Dawley strain male rats were purchased from Agricultural Research Center, Giza, Egypt. The average weight was 110 ± 10 g.

Methods

Preparation of Experimental Peels Powder: Fresh mango, apple and potato peels were washed three times with tap water and then dried at $70^\circ C$ for 5 h using a cross flow drier. The dried peel was powdered using a hammer mill then passed through a 0.5 mm sieve to obtain a fine powder and stored in freezer until use. 30 gm from each of these peels powder is added in diet in substitution of cellulose. 10 gm from mango, apple and potato peels were thoroughly shacked forming mixture of the experimental peels.

Biological Design: After adaptation period (one week), the rats were randomly classified into six groups of seven rats each. The first group served as a normal control group, fed on standard diet only. The other five groups were fed on standard diet and received 0.4 g/l of potassium bromate and 0.5 g/l cadmium chloride in drinking water and 5g/kg body weight/24h of ethanol in diet for four weeks according to previous studies [2, 6], then, Rats reclassified into 5 groups which were positive control (untreated) and treated rat groups that were mango, apple, potato and mixture peels groups. The treatment period is designed for four weeks. Food intake was calculated daily and the body weight gain was recorded weekly. Food efficiency ratio (FER) was determined by Chapman *et al.* [10] as following: FER = weight gain (g)/ food intake (g). At the end of experiment (8 weeks), the rats were anesthetized, blood sample were collected in clean centrifuge tubes. Half of blood were left for coagulation then centrifuged at 3000 rpm for 15 minutes to obtain serum. Livers and kidney for every rat were immediately removed and rinsed with saline, blotted on filter paper and divided into two halves. One half was stored at $-70^\circ C$ for biochemical analyses and the other was immersed in 10 % neutral buffered formalin as fixative and then sent to Pathological Department of Veterinary Medicine, Cairo University for histopathological examination.

Laboratory Analysis: Hemoglobin (Hg), packed cell volume (PCV), red blood cells (RBCs) and white blood cells (WBC_s) were determined according to Drabkin [11], MC-Inory [12] and Carleton [13], respectively. Serum alanine and aspartate aminotransferase (ALT&AST) and alkaline phosphatase (AP) enzymes activity; total protein (TP) and albumin were performed according to the method of Reitman and Frankel [14], Kind and King [15], Weichselbaum [16] and Bartholomev and Delany[17], respectively. Serum uric acid, creatinine and urea were determined according to Fossati *et al.* [18], Bonsens and Taussky, [19] and Patton and Crouch [20], respectively. Serum cholesterol, triglyceride (TG) and high density lipoprotein cholesterol (HDL_c) were estimated by an enzymatic colorimetric methods according to Richmond [21], Buccolo and David [22] and Grodon and Amer[23], respectively. Serum superoxide dismutase (SOD), glutathione peroxidase (GSP), catalase(CAT) and malondialdehyde (MDA) were determined by enzymatic colorimetric procedures according to Beuchamp and Fridovich [24], Flohe and Gunzler [25], Sinha [26] and Buege and Aust [27], respectively.

Calculation of Some Parameters: Serum globulin was calculated according to Coles [28] while very low density lipoprotein cholesterol (VLDL_c) and low density lipoprotein cholesterol (LDL_c) were calculated according to Lee and Nieman [29] as follows:

$$\begin{aligned} \text{Serum globulin} &= \text{total protein} - \text{albumin} \\ \text{VLDL}_c &= \text{TG} / 5 \\ \text{LDL}_c &= \text{total cholesterol} - \text{HDL}_c - \text{VLDL}_c \end{aligned}$$

Determination of Albumin / globulin (A/G) ratio and cholesterol /HDL_c ratio were calculated according to the methods Friedewald *et al.* [30] and Castelli and Levitar [31], respectively.

Histopathological Examination: The fixed samples of liver and kidney were cleared in xylol and embedded in paraffin. 4-5 μm thick section were prepared and stained with Hematoxylin and Eosin (H&E) for subsequent histopathological examination [32].

Statistical Analysis: All obtained data were statistically analyzed by SPSS computer soft ware. The calculated occur by analysis of variance ANOVA and follow up test LSD by SPSS ver. 11 according to Abo-Allam [33].

RESULTS

It can be noticed in Table 1 that positive control group showed only a significant increase in food efficiency ratio at p< 0.05 while mango group showed a significant decrease in weight gain (%) at p< 0.05 but apple group showed a significant decrease in final weight, FER (p< 0.01), weight gain and weight gain % at p<0.001 comparing with normal control group. Potato group showed a significant decrease in weight gain % at p< 0.05 but mixture group showed a significant decrease in final weight, weight gain (p< 0.05)and weight gain percent at p<0.01in comparing with normal control group. Mango and potato groups showed a significant decrease in weight gain % and FER while apple and mixture groups showed a significant decrease in final weight, weight gain, weight gain % and FER in comparing with positive control group.

Table 2 showed that positive control rat group showed a significant decrease in PCV, WBC_s (p< 0.01) and Hg and RBC_s at p<0.001 while mango, apple and potato groups showed a significant decrease in Hg and PCV at p< 0.05 in comparing with normal control group. All treated rat groups with mango, apple, potato and mixture peels revealed a significant increase in Hg, PCV, RBC_s and WBC_s in comparing with positive control group.

Table 1: Body weight gain, food intake and food efficiency ratio (FER) of the experimental rat groups

Groups Variables	Normal control	Positive control	Mango	Apple	Potato	Mixture
Initial weight(g)	119.8 ± 2.88 ^a	117.8 ± 3.31 ^a	117 ± 3.72 ^a	116.6 ± 4.24 ^a	117.2 ± 3.14 ^a	116.2 ± 2.40 ^a
Final weight(g)	167.6 ± 21.52 ^a	170.2 ± 29.46 ^a	157.8 ± 25.47 ^a	135.2 ± 19.48 ^{b***}	151.6 ± 25.08 ^{ab}	148.8 ± 26.28 ^{b*}
Weight gain(g)	47.8 ± 11.46 ^a	52.4 ± 14.57 ^a	40.8 ± 12.47 ^a	18.4 ± 4.51 ^{c***}	39.2 ± 7.62 ^{ab}	32.6 ± 7.70 ^{b*}
Weight gain%	44.90 ± 4.28 ^a	42.60 ± 4.36 ^a	36.30 ± 3.14 ^{b*}	17.40 ± 2.11 ^{d***}	37.30 ± 4.31 ^{b*}	26.50 ± 3.18 ^{c**}
Food intake(g)	14.37 ± 2.24 ^a	14.13 ± 3.68 ^a	13.95 ± 2.64 ^a	12.78 ± 2.28 ^a	13.57 ± 1.73 ^a	13.53 ± 3.05 ^a
FER	0.055 ± 0.001 ^b	0.061 ± 0.002 ^{a*}	0.048 ± 0.001 ^b	0.023 ± 0.003 ^{c**}	0.048 ± 0.001 ^b	0.040 ± 0.002 ^b

Significant with control group * P<0.05 ** P<0.01 *** P<0.001

Mean values in each raw having different superscript (a, b, c, d) are significant

Table 2: Blood levels of Hg, PCV, RBCs and WBCs of the experimental rat groups

Groups Variables	Normal Control	Positive control	Mango	Apple	Potato	Mixture
Hg (g/dl)	13.25± 0.96 ^a	9.15± 1.01 ^{****}	11.76± 0.40 ^{b*}	11.29 ± 0.68 ^{b*}	11.88± 0.10 ^{b*}	12.15± 0.97 ^{ab}
PCV (%)	39.02± 0.01 ^a	30.01± 0.01 ^{****}	36.11± 0.01 ^{b*}	35.12± 0.02 ^{b*}	36.20± 0.008 ^{**}	37.80± 0.02 ^{ab}
RBCs (Lµ/10 ⁶)	4.16± 0.59 ^a	3.42± 0.30 ^{b****}	4.34± 0.15 ^a	4.80± 0.28 ^a	4.37± 0.17 ^a	4.71± 0.33 ^a
WBCs (Lµ/10 ⁶)	7100± 308.14 ^b	6810± 466.90 ^{****}	8820± 487.27 ^b	7380± 344.24 ^b	7420± 756.31 ^b	7980± 593.29 ^b

Significant with control group * P<0.05 ** P<0.01 *** P<0.001

Mean values in each raw having different superscript (a, b, c, d) are significant

Table 3: Effect of experimental peels on liver functions parameters of the experimental rat groups

Groups Variables	Normal Control	Positive control	Mango	Apple	Potato	Mixture
ALT (µ/ml)	8.8± 2.86 ^b	17.4± 2.54 ^{****}	9.8± 2.77 ^b	10.2± 1.83 ^b	8.85± 1.30 ^b	9.4± 1.50 ^b
AST(µ/ml)	26.6± 8.20 ^b	56.4± 8.32 ^{****}	29.4± 2.60 ^b	21.2± 4.26 ^b	30.2± 5.89 ^b	22.2± 6.41 ^b
ALP(µ/ml)	104.4± 14.76 ^b	160.2± 15.73 ^{****}	116± 19.55 ^b	123.4± 14.44 ^b	129.6± 9.65 ^b	126.8± 17.85 ^b
T.P(g/dl)	7.08± 0.77 ^a	5.36± 0.43 ^{b**}	7.46± 0.60 ^a	7.1± 0.38 ^a	7.9± 0.56 ^a	7.42± 0.80 ^a
Albumin(g/dl)	3.96± 0.15 ^b	3.72± 0.64 ^b	4.18± 0.54 ^{a*}	3.3± 0.17 ^b	3.4± 0.31 ^b	3.02± 0.33 ^{bc}
Globulin(g/dl)	3.12± 0.66 ^b	1.64± 1.06 ^{c**}	3.28± 0.80 ^b	3.8± 0.43 ^{ab}	4.5± 0.71 ^{a*}	4.4± 0.97 ^{a*}
A/G ratio	1.26± 0.61 ^b	2.26± 0.51 ^{a**}	1.27± 0.35 ^b	0.86± 0.08 ^{c**}	0.77± 0.17 ^{c**}	0.72± 0.25 ^{c**}

Significant with control group * P<0.05 ** P<0.01 *** P<0.001

Mean values in each raw having different superscript (a, b, c, d) are significant

Table 4: Serum uric acid, creatinine and urea levels of the experimental rat groups

Groups Variables	Normal Control	Positive control	Mango	Apple	Potato	Mixture
Uric acid(mg/dl)	2.34± 0.37 ^b	4.86± 0.53 ^{****}	2.26± 0.54 ^b	2.72± 0.21 ^b	2.72± 0.45 ^b	2.46± 0.59 ^b
Creatinine(mg/dl)	0.47± 0.06 ^c	1.53± 0.01 ^{****}	0.44± 0.09 ^c	0.59± .03 ^{bc}	0.56± 0.11 ^{bc}	0.58± 0.03 ^{bc}
Urea(mg/dl)	26.40± 3.20 ^b	39.20± 5.83 ^{****}	26.60± 6.06 ^b	20.23± 3.70 ^{bc}	17.40± 2.81 ^{c**}	20.80± 3.70 ^{bc}

Significant with control group * P<0.05 ** P<0.01 *** P<0.001

Mean values in each raw having different superscript (a, b, c, d) are significant

Table 5: Serum SOD, GSP, catalase and MDA content of the experimental rat groups

Groups Variables	Normal Control	Positive control	Mango	Apple	Potato	Mixture
SOD (µ/ml)	0.71± 0.09 ^a	0.36± 0.09 ^{c****}	0.52± 0.03 ^{b*}	0.59± 0.05 ^{b*}	0.60± 0.05 ^{b*}	0.57± 0.18 ^{b*}
GSP (µ/ml)	0.90± 0.03 ^a	0.40± 0.08 ^{c****}	0.70± 0.01 ^{b*}	0.51± 0.01 ^{d****}	0.63± 0.01 ^{c*}	0.65± 0.14 ^{bc*}
Catalase (µ /ml)	1.16± 0.12 ^a	0.50± 0.12 ^{c****}	0.97± 0.09 ^{ab}	0.84± 0.07 ^{bc*}	0.60± 0.01 ^{c****}	0.71± 0.07 ^{d**}
MDA (mM /ml)	10.79± 0.57 ^c	17.17± 0.78 ^{****}	13.18± 1.13 ^{b*}	13.24± 0.58 ^{b*}	13.36± 0.47 ^{b*}	14.07± 1.33 ^{b*}

Significant with control group * P<0.05 ** P<0.01 *** P<0.001

Mean values in each raw having different superscript (a, b, c, d) are significant

Table 6: Some serum lipid parameters of the experimental rat groups

Groups Variables	Normal Control	Positive control	Mango	Apple	Potato	Mixture
Cholesterol(mg/dl)	118.12± 9.11 ^c	155.80± 8.43 ^{****}	132.40± 13.75 ^{b*}	148.60± 10.50 ^{b**}	120.71± 8.45 ^c	121.60± 9.78 ^c
Triglyceride(mg/dl)	137.22± 11 ^b	199.36± 15.16 ^{****}	123.61± 6.96 ^{bc}	120.60± 17.40 ^{bc}	125.40± 15.61 ^{bc}	112.40± 6.34 ^{ab**}
HDL _c (mg/dl)	49.31± 9.44 ^a	24.40± 6.87 ^{b****}	41.91± 10.48 ^a	40.80± 8.75 ^a	39.80± 12.69 ^a	41.20± 13.31 ^a
LDL _c (mg/dl)	41.60± 6.19 ^d	91.60± 10.34 ^{****}	66.80± 3.96 ^{c*}	83.68± .52 ^{b**}	55.12± 4.58 ^{cd}	57.92± 6.17 ^{cd}
VLDL _c (mg/dl)	27.40± 2.2 ^b	39.80± 3.03 ^{****}	24.60± 9.39 ^b	24.12± 9.48 ^b	25.08± 9.12 ^b	22.48± 1.26 ^b
Cholesterol / HDL _c	2.40± 0.98 ^b	6.38± 1.36 ^{****}	3.22± 1.01 ^b	3.64± 1.11 ^b	3.01± 1.02 ^b	2.95± 0.97 ^b

Significant with control group * P<0.05 ** P<0.01 *** P<0.001

Mean values in each raw having different superscript (a, b, c, d) are significant

The results in Table 3 showed that positive control group showed a significant increase in ALT, AST, ALP (p< 0.001) and albumin/globulin ratio (A/G) at p< 0.01 but a significant decrease in total protein (TP) and globulin at p< 0.01 in comparing with normal control group. Mango group showed a significant increase in albumin at p< 0.05 while apple group showed a significant decrease in A/G ratio at p< 0.01 in comparing with normal control group. Potato

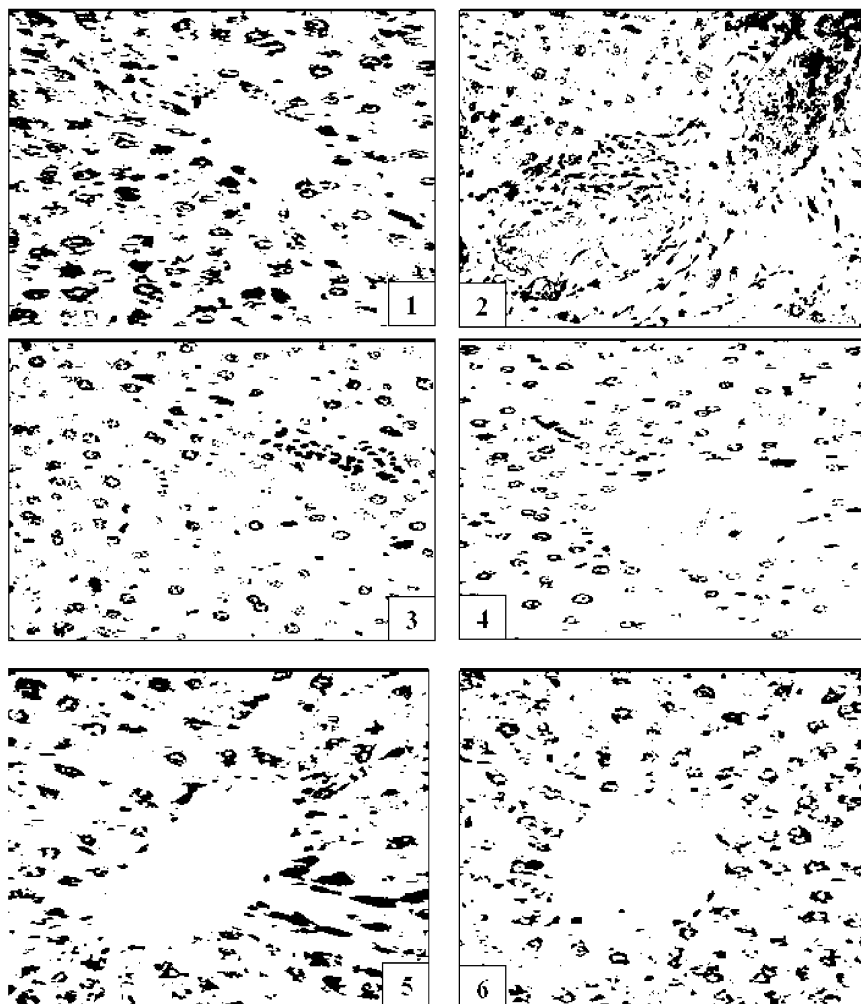
and mixture groups showed a significant increase in globulin at p< 0.05 but a significant decrease in A/G ratio at p< 0.01 in comparing with normal control group. Mango, apple, potato and mixture groups showed a significant decrease of ALT, AST, ALP and A/G ratio but a significant increase in total protein and globulin as well as mango group showed a significant increase in the value of albumin in comparing with positive control group.

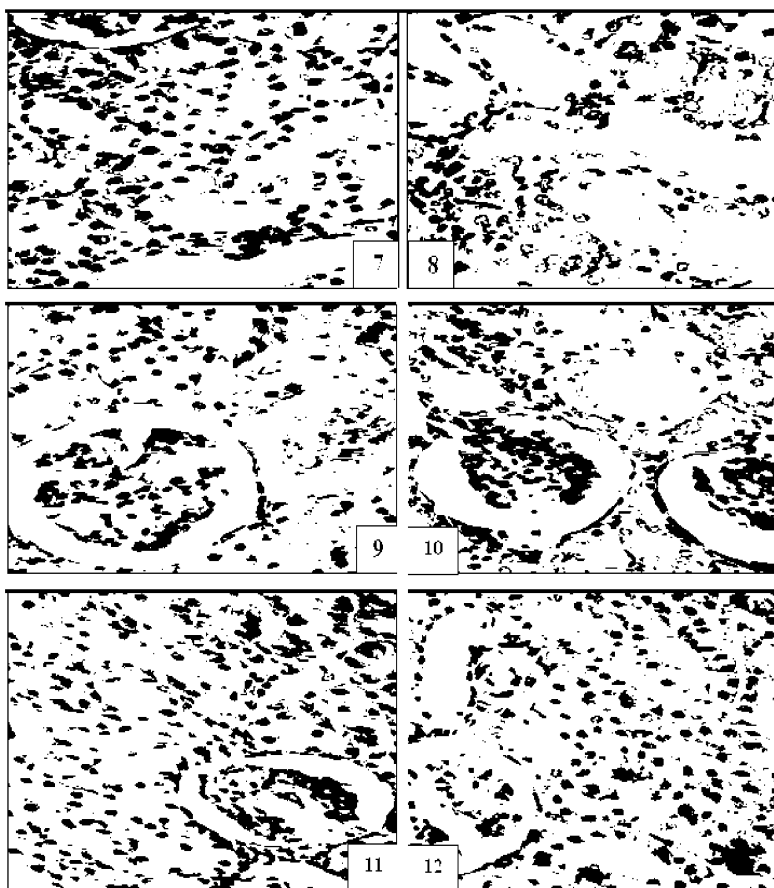
Data in Table 4 showed that positive control group showed a significant increase in uric acid, creatinine and urea at $p < 0.001$ while potato group showed a significant decrease in urea at $p < 0.01$ in comparing with normal control group. Mango, apple and mixture groups showed non significant difference in uric acid, creatinine and urea in comparing with normal control group. Mango, apple, potato peel and mixture groups revealed a significant decrease in uric acid, creatinine and urea levels in comparing with positive control group.

Table 5 showed positive control group showed a significant decrease in SOD, GSP and catalase at $p < 0.001$ but a significant increase in MDA at $p < 0.001$ in comparing with normal control group. Mango group showed a significant increase in MDA at $P < 0.05$ and a significant decrease in SOD and GSP at $p < 0.05$ but non significant decrease in catalase in comparing with normal control group. Apple peel ,potato peel and mixture rat groups showed a significant increase in MDA at $p < 0.05$

and a significant decrease in SOD, catalase and GSP at $p < 0.05, 0.001$ & 0.001 in comparing with normal control group. Mango, apple, potato peels and mixture rat groups revealed a significant increase in SOD, GSP and catalase and a significant decrease in MDA in comparing with positive control group.

The results in table (6) showed that positive control rat group showed a significant increase in cholesterol, triglyceride, LDLc ,VLDLc and cholesterol / HDLc at $p < 0.001$ but a significant decrease in HDLc at $p < 0.001$ in comparing with normal control group. Mango and apple groups showed a significant increase in cholesterol and LDLc at $p < 0.05$ & $p < 0.01$ while mixture group showed only a significant decrease in triglyceride at $p < 0.01$ in comparing with normal control group. Mango, apple, potato and mixture groups revealed a significant increase in HDLc but a significant decrease in cholesterol, triglyceride, LDLc, VLDLc and cholesterol/HDLc in comparing with positive control.





Histopathological Results: Microscopically, liver of rat from normal control group revealed the normal histological structure of hepatic lobule (Pict. 1), conversely, liver of rat from positive control group showed congestion of hepatoportal blood vessels, portal edema with leukocytic cells infiltration and pyknosis of their nucleous (Pict. 2). However, liver of rat from mango group showed sinusoidal leucocytosis (Pict. 3). Congestion of central vein was the only change observed in apple group (Pict. 4). Liver of rat from potato group showed no histopathological changes (Pict. 5). Besides, liver of rat from mixture group showing slight congestion of central vein (Pict. 6).

Microscopical examination of kidney of normal control group revealed the normal histological structure of renal parenchyma (Pict. 7). Meanwhile, kidney of rat from positive control group showed interstitial nephritis, cystic dilatation of renal tubules with eosinophilic protein cast (Pict. 8). However, kidney of mango group revealed congestion of renal blood vessel and hypertrophy of glomerular tuft (Pict. 9). Kidney of apple group revealed tubulo-interstitial nephritis (Pict. 10). No histopathological changes were noticed in kidney of potato group (Pict. 11).

Kidney of mixture group showed a slight congestion of renal blood vessel (Pict. 12).

DISCUSSION

Previous studies showed that cadmium causes tissue damage by membrane lipid peroxidation because of its ability to generate free radicals and inhibit antioxidant enzymes. Damage to cell membranes could lead to loss of membrane enzymes such as Na^+/K^+ ATPase, which is an important transport enzyme. It contributes to the development of serious pathological conditions because of its long retention time in some tissues [4]. Cadmium exposure has been considered to be potential cardiovascular risk factor, linked to an increased risk of myocardial infarction and diabetes mellitus type, as well as overall mortality [34]. After absorption of cadmium, it is delivered to the liver by endogenous intestinal metallothionein. Hepatic cadmium metallothionein then gradually redistributes the metal to the kidney, which is the main target organ for chronic cadmium toxicity. The cadmium-induced inhibition of many metalloenzymes is reported to be the result of the displacement of metals

from the active site of the enzymes. Superoxide dismutase is a metalloenzyme and inhibited in the tissues of cadmium-treated rats. The decrease in SOD activity would diminish the ability of the tissues to scavenge free radicals, which could have accounted for the increase in membrane lipid peroxidation in the tissues of the rats [35].

Chronic exposures to KBrO₃ cause renal cell tumors in rats. Bromate mediates toxicological effects via the induction of oxidative stress. The carcinogenic doses of potassium bromate require attainment of a threshold at which oxidation of tissues occurs and that gene expression profiles may be predictive of these physiological changes in renal homeostasis [3]. The decline in renal mitochondrial function following a subchronic and chronic exposure to potassium bromate based on the oxidative stress mode-of-action of bromate. Bromate toxicity in male rat kidney includes changes in energy consumption and utilization in renal cells that involve up-regulation of glycolytic processes, possibly resulting from altered mitochondrial function [36].

Ethanol is primarily metabolized, or oxidized in the hepatic microsome into acetaldehyde then further oxidized into acetic acid. This two step oxidizing process releases protons which would reduce NAD⁺ into energy potent NADH [5]. Ethanol administration also elicits hepatic disturbances in the availability of non-safely-sequestered iron derivatives and in the antioxidant defense. The resulting oxidative stress leads, in some experimental conditions, to enhanced lipid peroxidation and can also affect other important cellular components, such as proteins or DNA [37]. Ethanol intoxication is accompanied by changes in the composition of liver cell membranes, which leads to changes in membrane symmetry, fluidity and other properties. Ethanol toxicity in liver is directly linked to the depletion of glutathione [38]. Chronic ethanol consumption has been closely associated with liver steatosis and its subsequent injury caused by increased hepatic lipid concentrations [39]. The liver is the main site of ethanol biotransformation and a target organ of the xenobiotic, but the kidney is the main site of cadmium accumulation and a target organ of the metal. Ethanol intoxication is accompanied by changes in the composition of liver cell membranes, which leads to changes in membrane symmetry, fluidity and other properties. Ethanol makes the organism more susceptible to cadmium accumulation and toxicity [40]. Xenobiotics increase glutathione transferase isozymes and little or no increase in peroxidase activity in rat liver cytosolic. The depression of selenium-dependent glutathione peroxidase activity following sustained induction of glutathione

transferases may have direct implications for the toxicity of the polyhalogenated aromatic hydrocarbons [38].

Erythrocytes are prone to oxidative stress because they are exposed to high oxygen tension and have polyunsaturated fatty acid in the membrane and hemoglobin-bound iron. Free radical-catalyzed peroxidative damage to membrane lipids may impair the erythrocyte deformability and metabolic machinery that resulting in decreased ATP level and cause oxidative hemolysis. Oxidative damage to membrane can permit leakage of free denatured hemoglobin, which may form nephrotoxic hemoglobin, leading to kidney damage [41]. Erythrocytes have an efficient antioxidant mechanism to scavenge ROS and maintain their integrity. A detoxifying system consisting of reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase and vitamin E prevents oxidative damage and repair oxidative damage [42]. Free radical-mediated lipid peroxidation induced by these chemicals play a crucial role in various steps that initiate and regulate the progression of liver diseases [43]. Malondialdehyde is a naturally occurring product of lipid peroxidation and prostaglandin biosynthesis that is mutagenic and carcinogenic. It is an indicator of lipid peroxidation provides a reasonable marker for free radical induced protein oxidation. Lipid peroxidation may lead to DNA damage, membrane damage, altered gene expression and apoptosis [44]. Peels are the major by-products obtained during the processing of various fruits and these were shown to be a good source of polyphenols, carotenoids and other bioactive compounds which posses various beneficial effects on human health [45,46]. Mango peels is a major by-product in pulp industry and it appeared rich in pectins, uronic acids, galactose, arabinose and rhamnose. Mango peels originating from fruit processing are a promising source of phenolic compounds that might be recovered and used as natural antioxidants or functional food ingredients [47]. Mango peel contains various bioactive compounds like polyphenols, carotenoids and others. The oxidative hemolysis of rat erythrocytes by hydrogen peroxide was inhibited by mango peel extract in a dose dependent manner. The mango peel extract showed protection against membrane protein degradation caused by hydrogen peroxide. Diets containing high fiber content have been reported to decrease absorption of cadmium [48, 49].

Apples are a good source of phenolic compounds, especially the skin, is rich in many health-enhancing phytonutrients including flavonoids and phenolic acids [50]. The phenolic compound composition and antioxidant

properties of 21 selected apple genotypes were evaluated. The apple skin extracts were revealed to be effective inhibitors of oxidation of polyunsaturated fatty acid in a model system and thus can be considered as a potential source of natural food antioxidants. The peel expresses a significantly higher concentration of phenolics compared to the flesh [51, 52]. Potato peel, a waste by-product from potato processing, could be considered as a new source of natural antioxidant. Potato peel is found to contain phenolic acids and recently the antioxidant activity of potato peel extract has been studied in food systems [53]. Potato peel provides an excellent source for the recovery of phenolic compounds, since almost 50% of phenolics are located in the peel and adjoining tissues and decrease toward the center of the tuber [54]. Effectiveness of extraction, stability and activity of the phenolic compounds and their suitability for food use are the important considerations in their recovery and utilization from industrial byproduct [55]. The bioactive materials were extracted with methanol and examined for their antioxidant activity potato peels under accelerated oxidation conditions, using sunflower and soybean oils as oxidation substrates at different concentrations for 72 h at 70°C. Potato peel is a potent source of natural antioxidants that might be explored to prevent oxidation of vegetable oils [56].

It is concluded that the peels under study (mango, apple and potato peels) may impart health benefits against oxidative stress and it could be used as a valuable food ingredient or a nutraceutical product.

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