

Red Ginseng Extract and Selenium Reduce Oxidative Stress Induced by Potassium Bromate in Male Rats

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ABSTRACT

The effect of red ginseng extract (RGE) and selenium (Se) on potassium bromate (KBrO₃)-induced oxidative stress in rats was investigated. Fifty mature male rats were used in this study and randomly distributed into 5 groups (n=10). Group (1) was kept as a negative control and the other 4 groups were injected with a single intraperitoneal dose of KBrO₃ (125 mg/kg/BW) to induce oxidative stress. Group (2) was kept as a positive control and groups (3), (4) and (5) were orally given RGE (200 mg/kg/ BW), Se (0.5 mg/kg/ BW) and RGE and Se, daily for 8 weeks, respectively. At the end of experiment, blood samples were collected and livers were taken for biochemical analyses. The results showed that oxidative stress induced by KBrO₃ in rats caused significant decreases in body weight gain and feed efficiency ratio. It also passively affected biomarkers of hepatorenal function, increased lipid peroxidation and decreased the activity of antioxidant enzymes (GPX, SOD and CAT) in liver tissues. Oral administration of RGE increased weight gain and feed efficiency ratio. RGE also improved hepatorenal function, decreased lipid peroxidation and normalized biomarkers of oxidative stress. These effects were amplified by coadministration of red ginseng extract with selenium and this might be attributed to the addition effect. In conclusion, coadministration of red ginseng plant and selenium induces high antioxidant activity as it markedly reduces oxidative stress biomarkers in rats. Therefore intake of red ginseng and selenium may be beneficial for patients with oxidative stress which is linked as a main cause of many diseases.

Key words: Red Ginseng; Selenium; Oxidative stress; Potassium bromate Antioxidants; Hepatorenal function; Biochemistry; Rats.

INTRODUCTION

Oxidative stress is a state in which oxidation exceeds the antioxidant systems in the body. Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses against them, which induces cellular damage. The antioxidant defenses enable the body system to remove ROS, restore the prevailing reducing environment and repair the tissue damage (Halliwell and Gutteridge, 1999). Free radicals such as nitric oxide (NO) and superoxide ions are produced as second messengers, particularly by immune cells. Superoxide reacts rapidly with nitric oxide by nitric oxide synthase to produce peroxynitrite, whereas hydrogen peroxide (H₂O₂) slowly decomposes to the highly reactive hydroxyl radical. Both peroxynitrite and hydroxyl radicals are highly reactive oxidizing agents, capable of damaging proteins, lipids, and DNA (Beckman and Koppenol, 1996). Oxidative stress plays an important role in the etiology and pathogenesis of many chronic diseases such as atherosclerosis, hypertension, diabetes mellitus, and cancers (Reuter *et al.*, 2010 and Krajcovicova-Kudlackova, *et al.*, 2012).

Potassium bromate (KBrO₃) is widely used as a food additive in the bread making processes and found in drinking water samples as a by-product of

ozone disinfection. KBrO₃ causes renal cell cancer and act as a tumor promoter in carcinogen-initiated animals. Renal cell tumors have been observed in rats after exposure to this compound due to oxidative stress induced by KBrO₃ (Fuji *et al.*, 1984 and Kurokawa *et al.*, 1990).

Dietary intake of antioxidants can inhibit or delay the oxidation of susceptible cellular substrates so prevent oxidative stress. Phenolic compounds such as flavonoids, phenolic acids, diterpenes, saponins and tannins have received much attention for their high antioxidative activity (Rice-Evan *et al.*, 1996). Therefore, it is important to enrich our diet with antioxidants to protect our body against many chronic diseases. Moreover, antioxidants play an important role in food quality preservation due to their ability to prevent oxidative deterioration of lipids (Erukainure *et al.*, 2012).

Red ginseng is one of slow growing perennial plant with fleshy roots, belonging to genus *Panax* of family *Araliaceae*. Its roots are rich in glycosylated saponins named ginsenosides which have been reported to produce various biological activities. Different extracts red ginseng roots were found to produce hypoglycemic and antidiabetic effects (Ng and Yeung, 1985; Takaku *et al.*, 1990 and Kim and Kim, 2008); hepatoprotective action (Lee *et al.*, 2005) and hypocholesterolemic and hypolipidemic

activities (Kawak *et al.*, 2010 and Shin *et al.*, 2011) in man and experimental animals.

Selenium is an essential trace element and micronutrient that in very small amounts is essential for good health and normal physiological functions. Selenium is a component of the antioxidant enzyme glutathione peroxidase. It is a key component of the antioxidant defense against reactive oxygen species (Rayman, 2000). Selenium produces antioxidant effect by its direct antioxidant effect, synthesis of glutathione peroxidase and other antioxidant enzymes and repair of proteins (Thomson, 2004). Selenium is found in minute amounts in foods and the richest sources are being from meat, seafood, whole grains, nuts, vegetables and dairy products (Yiming *et al.*, 2005).

The present study aimed to investigate the effect of coadministration of red ginseng extract with selenium on oxidative stress induced by potassium bromate in male rats.

MATERIALS AND METHODS

1. Plant

Dried roots of red ginseng (Family *Araliaceae*) were purchased from a local market of Agricultural Herbs, Spices and Medicinal plants, Cairo, Egypt. These roots of the plant were authenticated in Botany Department, Faculty of Agriculture, Cairo University. The dried roots of red ginseng were grinded using a coffee grinder into a fine powder before extraction.

2. Rats

Fifty mature male rats of Sprague Dawley strain weighing 175 ± 5 g each and 10-12 weeks old were obtained from the Laboratory Animals Farm, Helwan, Egypt. The rats were housed at a controlled room temperature of $23 \pm 1^\circ\text{C}$, 55 % humidity and under a 12-hr light / 12-hr dark schedule. The animals were fed on basal diet and water was provided *ad libitum* for one week before the start of experiment for acclimatization.

3. Chemicals

Potassium bromate (KBrO₃) in the form of white powder (soluble in boiling water) was purchased from El-Gomhoryia Company, Cairo Egypt. Selenium (Se) as sodium selenite powder was supplied from Sigma-Aldrich Chemie GmbH, West Germany. Biochemical kits for the determination of liver enzymes AST, ALT and urea nitrogen, uric acid, creatinine, total cholesterol and triglycerides were purchased from Alkan Company for Chemicals and Biodiagnostics, Dokki, Cairo, Egypt.

4. Preparation of red ginseng extract

Red ginseng alcoholic extract was prepared by soaking 200 g of the dry roots in 1 liter of 90% ethyl alcohol and kept in a refrigerator with daily shaking for 5 days. The ethanol was evaporated using a rotatory evaporator apparatus (manufactured in

West Germany) attached with a vacuum pump. Twenty grams of the obtained semisolid extract were suspended in distilled water with 2ml of Tween 80 (suspending agent) and 80 ml of distilled water were gradually added to prepare a 20% liquid extract.

5. Preparation of basal diet

The basal diet was prepared using AIN-93 according to Reeves *et al.* (1993). 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%.

6. Experiment and grouping of rats

After one week adaptation period, the animals were randomly allocated into five equal groups, of 10 rats each. Group (1) was fed on basal diet and kept without any treatment as a negative control. The other four groups were injected by a single intraperitoneal dose of potassium bromate at dose of 125 mg/kg BW for induction of oxidative stress (Khan and Sultana 2004). Group (2) was left as a positive control and groups (3), (4) and (5) were given orally red ginseng extract (RGE) at a dose 200 mg/kg, selenium (Se) at 0.5 mg/kg and RGE with Se, respectively, daily for 8 weeks.

The food intake was calculated daily and the body weight gain was recorded weekly (Chapman *et al.*, 1950). Feed efficiency ratio (FER) was calculated as $\text{FER} = \text{weight gain (g)} / \text{feed intake (g)}$. At the end of experiment (8 weeks), the rats were anesthetized using ether anesthetic and blood samples were collected into clean centrifuge tubes to obtain the serum which used for biochemical analyses. Livers of all rats were immediately removed, rinsed with saline, blotted on filter paper and stored at -70°C pending for the preparation of liver homogenate for biochemical assays.

7. Biochemical analyses

Activities of serum liver enzymes aspartate and alanine aminotransferases (AST and ALT) were chemically determined according to Bergmeyer *et al.* (1978). Serum total cholesterol (Ratliff and Hall, 1973) and triglycerides (Jacob and Van-Denmark, 1963) were chemically determined. Blood urea nitrogen (BUN) was determined using BioMérieux kits according to Patton and Crouch (1977). Serum uric acid was determined using the enzymatic colorimetric method as described by Fossati *et al.* (1980). Serum creatinine concentrations were colorimetrically determined by the Jaffe reaction (Husdan and Rapoport, 1968). Serum lipid peroxide malondialdehyde (MDA) and reduced glutathione (GSH) contents were estimated according to methods described by Placer *et al.* (1966) and Afzal *et al.* (2002), respectively.

8. Preparation of liver homogenate

One gram of frozen liver tissue was collected, washed in ice-cold 0.9% NaCl and homogenized in ice-cold 1.15% solution of potassium chloride and 50 mM potassium phosphate buffer solution (pH 7.4) to yield 10% homogenate (W/V). Homogenization was performed using ultrasonic homogenizer (Sonicator, model 4710, Cole-Parmer Instrument Company, USA). The homogenate was then centrifuged at 4000 rpm for 15 minutes at 4°C and the supernatant was collected for further use.

9. Lipid peroxidation and tissue antioxidant enzymes

Lipid peroxidation (LPO) was determined by quantifying malondialdehyde (MDA) that formed in terms of thiobarbituric acid reactive substances (TBARS). Liver homogenate was used for determination of tissue lipid peroxide (MDA), enzymatic (GPx, SOD and CAT) and non enzymatic (GSH) antioxidants. The reduced glutathione (GSH) content in liver homogenate was determined colorimetrically by the method modified by Bulaj *et al.* (1998). Lipid peroxide (MDA) was determined according to Ohkawa *et al.* (1979). The activities of glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT) antioxidant enzymes were determined chemically according to Paglia and Valentine (1979), Spitz and Oberley (1989) and Sinha (1972), respectively.

10. Statistical analysis

Data were presented as means \pm SD and statistically analyzed using one way analysis of variance (ANOVA) test followed by Duncan's multiple range test. Differences between control and treated groups were considered significant at $P < 0.05$ level (Snedecor and Cochran, 1986) using computerized SPSS program.

RESULTS

Intraperitoneal injection of potassium bromate in a single (125mg/kg BW) dose to rats caused significant ($P < 0.05$ and $P < 0.01$) decreases in body

weight gain, food intake and feed efficiency ratio (FER) when compared to the negative control group. In rats with oxidative stress, the oral administration of red ginseng extract and selenium, alone and in combination, for 8 weeks caused significant ($P < 0.05$ and $P < 0.001$) increases in bodyweight gain, food intake and FER when compared with the positive control group. Administration of both red ginseng extract and selenium together produce the best effect on body weight gain and feed efficiency (FER) when compared to administration of red ginseng or selenium alone as recorded in Table (1).

As shown in Table (2) the rats injected with potassium bromate had significant ($P < 0.01$ and $P < 0.001$) increases in serum levels of AST, ALT, total cholesterol (TC) and triglycerides (TG) when compared to the negative control group. Oral administration of red ginseng extract and selenium, alone and in combination, to rats with oxidative stress produced significant ($P < 0.05$ and $P < 0.01$) decreases in the elevated serum levels of AST, ALT, TC and TG when compared with the positive control group. The best lowering effect on the activity of serum AST enzyme and level of TC and TG was by administration of both red ginseng extract and selenium together when compared with their administration alone.

Rats with oxidative stress had significant ($P < 0.05$ and $P < 0.001$) increases in urea nitrogen (UN), uric acid (UA) and creatinine (Cr) levels in the serum when compared to negative control rats. Oral administration of red ginseng extract and selenium alone and in combination to rats with oxidative stress produced significant ($P < 0.01$) decreases of the elevated serum UN, UA and Cr. concentrations when compared with the positive control group. Coadministration of both red ginseng extract and selenium produced the best lowering effect on serum urea nitrogen when compared with their administration alone as recorded in Table (3).

Table 1: Effect of red ginseng extract (RGE) and selenium on body weight gain, feed intake and feed efficiency ratio (FER) in rats with oxidative stress.

Groups Parameters	Control (-ve)	Control (+ve)	RGE (200mg/kg)	Selenium (0.5 mg/kg)	RGE+ Selenium
Initial weight (g)	174.00 $\pm 6.24^a$	179.50 $\pm 6.31^a$	175.00 $\pm 5.21^a$	179.50 $\pm 4.36^a$	180.00 $\pm 4.66^a$
Final weight (g)	263.27 $\pm 16.76^a$	215.36 $\pm 12.71^{b*}$	242.06 $\pm 13.88^a$	244.19 $\pm 15.66^a$	252.49 $\pm 14.28^{c*}$
Weight gain (g)	88.23 $\pm 6.65^a$	34.75 $\pm 3.21^{c***}$	60.75 $\pm 6.11^{b*}$	62.88 $\pm 7.13^{b*}$	73.14 $\pm 8.11^{c*}$
Feed intake (g/w)	19.30 $\pm 1.26^a$	15.74 $\pm 1.21^{b*}$	19.25 $\pm 1.31^{b*}$	18.88 $\pm 1.21^{b*}$	19.20 $\pm 1.25^{c*}$
FER	0.075 $\pm 0.003^a$	0.032 $\pm 0.004^{d***}$	0.051 $\pm 0.001^{c**}$	0.055 $\pm 0.002^{c**}$	0.069 $\pm 0.004^{b***}$

Mean \pm SD values in each row with different superscripts (a, b, c, d) are significant when compared to the control groups at * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$ n = 10 rats/group.

Table 2: Effect of red ginseng extract (RGE) and selenium on serum AST, ALT, total cholesterol (TC) and triglycerides (TG) in rats with oxidative stress.

Groups Parameters	Control (-ve)	Control (+ve)	RGE (200mg/kg)	Selenium (0.5 mg/kg)	RGE+ selenium
AST (U/dl)	65.36 ± 3.71 ^c	89.11 ± 5.91 ^{a***}	78.21 ± 5.11 ^{b*}	76.31 ± 3.98 ^{b*}	67.31 ± 3.98 ^{b*}
ALT (U/dl)	35.22 ± 2.11 ^c	58.66 ± 3.71 ^{a***}	48.66 ± 3.71 ^{b*}	45.19 ± 5.66 ^{b*}	39.49 ± 4.28 ^{c*}
TC (mg/dl)	112.9 ± 3.22 ^d	132.5 ± 2.44 ^{a***}	126.4 ± 3.15 ^{b**}	124.3 ± 2.13 ^{b*}	118.4 ± 1.16 ^{c***}
TG (mg/dl)	95.6 ± 2.12 ^d	119.3 ± 3.14 ^{a***}	114.4 ± 2.52 ^{b**}	112.7 ± 2.41 ^{b*}	102.3 ± 1.90 ^{c***}

Mean ± SD values in each row with different superscripts (a, b, c) are significant

Significant when compared to the control groups at * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$ n = 10 rats/group.

Table 3: Effect of red ginseng extract (RGE) and selenium on urea nitrogen, uric acid and creatinine concentrations in rats with oxidative stress.

Groups Parameters	Control (-ve)	Control (+ve)	RGE (200mg/kg)	Selenium (0.5 mg/kg)	RGE+ selenium
Urea nitrogen (mg/dl)	36.45 ± 2.34 ^d	68.56 ± 2.54 ^{a***}	42.75 ± 6.11 ^{b*}	39.88 ± 7.13 ^{b*}	37.14 ± 8.11 ^{c*}
Uric acid (mg/dl)	1.35 ± 0.12 ^d	2.55 ± 0.17 ^{a**}	1.90 ± 0.15 ^{b**}	1.75 ± 0.13 ^{b**}	1.60 ± 0.16 ^{c**}
Creatinine (mg/dl)	1.10 ± 0.02 ^d	1.60 ± 0.04 ^{a**}	1.40 ± 0.02 ^{b**}	1.35 ± 0.01 ^{b**}	1.20 ± 0.0 ^{b**}

Mean ± SD values in each row with different superscripts (a, b, c, d) are significant when compared to the control groups at * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$ n = 10 rats/group.

Data in Table (4) showed that injection of potassium bromate to rats caused an elevation in serum level of lipid peroxide malondialdehyde (MDA) and lowering level of reduced glutathione (GSH) as compared with negative control rats. Red ginseng and selenium when given together orally to rats with oxidative stress induced a significant ($P < 0.05$ and $P < 0.001$) decrease in MDA and an increase in GSH levels in the serum when compared with the positive control group. Administration of both red ginseng extract and selenium together caused the best increase in serum MDA level when compared to their administration alone.

In liver tissues of rats with oxidative stress, there was a significant ($P < 0.01$ and $P < 0.001$) increase in levels of MDA and decrease in levels of

GSH when compared with the negative control group. Oral coadministration of red ginseng with selenium significantly reduced liver MDA level and increased GSH level when compared with the positive control group as shown in Table (5).

Concerning the activity of antioxidant enzymes, the rats with oxidative stress had decreased activity of glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT) enzymes in liver tissues as compared to the negative control group. Oral coadministration of red ginseng with selenium caused significant ($P < 0.01$ and $P < 0.001$) increases in the activity of GPx, SOD, CAT enzymes in liver tissues as compared with the positive control group (Table 6).

Table 4: Effect of red ginseng extract (RGE) and selenium on serum malondialdehyde (MDA) and reduced glutathione (GSH) in rats with oxidative stress.

Groups Parameters	Control (-ve)	Control (+ve)	RGE (200mg/kg)	Selenium (0.5 mg/kg)	RGE+ Selenium
MDA (mmol/ml)	35.22 ± 2.11 ^d	58.66 ± 3.71 ^{a***}	48.66 ± 2.23 ^{b*}	45.19 ± 2.66 ^{b*}	39.49 ± 2.28 ^{c*}
GSH (mmol/ml)	65.36 ± 3.71 ^b	49.11 ± 5.91 ^{d***}	58.21 ± 5.11 ^{c**}	62.31 ± 3.98 ^{b**}	70.31 ± 3.98 ^{a***}

Mean ± SD values in each row with different superscripts (a, b, c, d) are significant

Significant when compared to the control groups at * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$ n = 10 rats/group.

Table 5: Effect of red ginseng extract (RGE) and selenium on liver malondialdehyde (MDA) and reduced glutathione (GSH) in rats with oxidative stress.

Parameters	Control (-ve)	Control (+ve)	RGE (200mg/kg)	Selenium (0.5 mg/kg)	RGE+ selenium
MDA (nmol/min/mg protein)	0.26 ± 0.002 ^d	0.72 ± 0.003 ^{a***}	0.55 ± 0.001 ^{b**}	0.45 ± 0.003 ^{b**}	0.32 ± 0.002 ^{c***}
GSH (nmol/min/mg protein)	22.4 ± 1.25 ^a	10.4 ± 1.15 ^{d***}	18.36 ± 2.71 ^{b*}	19.19 ± 2.66 ^{b**}	21.49 ± 3.28 ^{c***}

Mean ± SD values in each row with different superscripts (a, b, c, d) are significant when compared to the control groups at * $P < 0.01$ ** $P < 0.01$ *** $P < 0.001$ n = 10 rats/group.

Table 6: Effect of red ginseng extract (RGE) and selenium on the activity of antioxidant enzymes in liver tissues of rats with oxidative stress.

Parameters	Control (-ve)	Control (+ve)	RGE (200mg/kg)	Selenium (0.5 mg/kg)	RGE+ selenium
GPx (nmol/min/mg protein)	0.60 ± 0.02 ^a	0.16 ± 0.01 ^{d***}	0.35 ± 0.003 ^{b*}	0.45 ± 0.002 ^{b**}	0.54 ± 0.001 ^{c**}
SOD (U/mg protein)	55.73 ± 1.25 ^a	30.82 ± 1.25 ^{d***}	42.36 ± 2.71 ^{b**}	49.19 ± 2.66 ^{b**}	52.49 ± 1.28 ^{c***}
CAT (nmol/min/mg protein)	0.188 ± 0.003 ^a	0.136 ± 0.002 ^{d***}	0.154 ± 0.001 ^{b**}	0.162 ± 0.002 ^{b**}	0.172 ± 0.001 ^{c**}

Mean ± SD values in each row with different superscripts (a, b, c, d) are significant when compared to the control groups at * $P < 0.01$ ** $P < 0.01$ *** $P < 0.001$ n = 10 rats/group.

DISCUSSION

The present study was carried out to investigate the effect of coadministration of red ginseng extract (RGE) with selenium (Se) on oxidative stress induced by potassium bromate (KBrO₃) in male rats.

The results showed that oxidative stress induced by KBrO₃ in rats was characterized by a reduction in body weight gain and feed efficiency, an increase in lipid peroxidation and elevation in serum and liver biochemical markers of oxidative stress. These findings were partially similar to those obtained by Abd El-Ghany *et al.* (2011) who reported that serum bilirubin was greatly increased, while the total proteins were significantly decreased in bromobenzene-treated rats when compared to the untreated control group. These findings indicated an injury, impaired function and damage of liver cells because of oral ingestion of bromobenzene. The authors reported a decline in renal mitochondrial function following subchronic and chronic exposure to potassium bromate based on the oxidative stress action of bromate. The bromate toxicity in male rat kidney included changes in energy consumption and utilization in renal cells that involved up-regulation of glycolytic processes, possibly resulting from altered mitochondrial function. Oral ingestion of bromobenzene induced hepatotoxicity that evident from a significant elevation of activities of AST and ALT in male rats with bromobenzene- induced hepatotoxicity (El-Sharaky *et al.*, 2009).

Lipid peroxidation is a complex process that damages the cell structure and function. Peroxidation of cell membrane lipids initiates a loss of membrane integrity; membrane bound enzyme activity and cell lyses. Oxidative damage in tissues

can be limited by the defense system of the host. These defenses appear to be inducible by nutrient and non nutrient antioxidants. Low levels of tissue antioxidant enzymes are likely to result in a tissue damage caused by lipid peroxides or protein carbonyls (Pryor and Squadrito, 1995). The increased lipid peroxidation due to oxidative stress induced by potassium bromate in this study was similar to that previously reported by Kurokawa *et al.* (1990), Khan and Sultana (2004) and Abd El-Ghany *et al.* (2011).

Results of the current study revealed that oral administration of red ginseng extract (RGE) to rats with oxidative stress induce by potassium bromate (KBrO₃) improved hepatorenal function, reduced lipid peroxidation and produced high antioxidant activity. Many medicinal plants were found to possess bioactive constituents which produce high antioxidant activity and prevent oxidation of lipids. Various phenolic compounds such as flavonoids, phenolic acids, diterpenes, saponins and tannins possess diverse biological activities and are thought to be beneficial for reducing cell damage induced by oxidative stress. The activity of phenolic compounds might be related to their antioxidant effect due to their ability to scavenge the free radicals by presence of hydroxyl groups in these compounds (Djeridane *et al.*, 2006). The hepatoprotective action of RGE reported in the present study was similar to that obtained by Lee *et al.* (2005). Hypocholesterolemic and hypolipidemic effects of RGE were in accordance with those reported by Jeong *et al.* (1997), Kim *et al.* (2005), Kawak *et al.* (2010) and Shin *et al.* (2011). The antioxidant effect of RGE, reported herein, agreed

with that previously reported by Khan and Sultana (2004) and Lee *et al.* (2005). The present results also showed that the antioxidant effect of RGE was amplified by its coadministration with selenium.

Selenium (Se) is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes. The antioxidant properties of selenoproteins help to prevent cellular damage from free radicals. However, other selenoproteins regulate thyroid function and play an important role in the immune system (McKenzie *et al.*, 1998). It is well known that Se is a component of the enzyme glutathione peroxidase that helps to induce and maintain the glutathione antioxidant system (Combs and Gray 1998). The antioxidant effects of Se can also be accounted for its role in the selenium-dependent thioredoxin reductase and plays an important role in the functioning of the thyroid gland (Kohrle *et al.*, 2005). In addition, Se is a key component of the antioxidant defense against reactive oxygen species (Rayman, 2000). The mechanisms of antioxidant activity of Se might be due to its direct antioxidant effect, its sharing synthesis of glutathione peroxidase and other antioxidant enzymes and its repairing effect of proteins (Thomson, 2004).

In conclusion, the results suggest that oral administration of red ginseng extract to rats with oxidative stress improves hepatorenal function, reduces lipid peroxidation and produces high antioxidant activity. These effects are amplified by coadministration of red ginseng extract with selenium. Therefore, intake of red ginseng with selenium may be beneficial for reducing the oxidative stress which is linked as a main cause of many diseases.

REFERENCES

- Abd El-Ghany, M.; Ramadan, A. and Hassan, S. (2011): Antioxidant activity of some agro-industrial peels on liver and kidney of rats exposed to oxidative stress. *World J. Dairy Food Sci.*; **6** (1):105-114.
- Afzal, M.; Afzal, A.; Jones, A. and Armstrong, D. (2002): A rapid method for the quantification of GSH and GSSG in biological samples. Cited in: "Oxidative stress biomarkers and antioxidant protocol". Editor Armstrong D., Humana Press, Page 117–122.
- Beckman, J.S. and Koppenol, W.H. (1996): Nitric oxide, superoxide, and peroxynitrite: the good, the bad, and ugly. *Am. J. Physiol.*; **271**: 1424-1437.
- Bergmeyer, H.U.; Schreiber, P. and Wahlefeld, A.W. (1978): Optimization of methods for aspartate and alanine aminotransferases. *Clin. Chem.*; **24**: 58-61.
- Bulaj, G.; Kortemme, T. and Goldenberg, D. (1998): Ionization-reactivity relationship for cystine thiols in polypeptides. *Biochem.*; **37**: 8965- 8972.
- Chapman, D.G.; Gastilla, R. and Campbell, T.A. (1950): Evaluation of protein in food: A method for the determination of protein efficiency ratio. *Can. J. Biochem. Physiol.*; **37**: 679-686.
- Combs, G.F. and Gray, W.P. (1998): Chemopreventive agents: Selenium. *Pharmacol. Therap.*; **79**:179-192.
- Djeridane, A.; Youssef, M.; Nadjemi, B.; Boutassouna, D.; Stocker, P. and Vidal, N. (2006): Antioxidant activity of some Algerian medicinal plant extracts containing phenolic compounds. *Food Chem.*; **97**: 654-660.
- El-Sharaky, A.S.; Newairy, A.A.; Kamel, M.A. and Eweda, S.M. (2009): Protective effect of ginger extract against bromobenzene-induced hepatotoxicity in male rats. *Food Chem. Toxicol.*; **47**: 1584-1590.
- Erukainure, O.L.; Oke, O.V.; Owolabi, F.O.; Kayode, F.O.; Umanhonlen, E.E. and Aliyu, M. (2012): Chemical properties of *Monodora myristica* and its protective potential against free radicals *in vitro*. *Oxid. Antioxid. Med. Sci.*; **1**(2): 127-132.
- Fossati, P.; Prencipe, L. and Berti, G. (1980): Use of 3, 5 dichloro-2- hydroxyl benzene sulfonic acid /4-amyphenazone chromogenic system in direct enzymatic assay of uric acid in serum and urine. *Clin. Chem.*; **26**: 227-231.
- Fuji, M.; Oikawa, K.; Saito, H.; Fukuhara, C. and Tanaka, K. (1984): Metabolism of potassium bromate in rats: *In vitro* studies. *Chemosphere*; **13**: 1207-1212.
- Halliwell, B. and Gutteridge, J. (1999): "Free Radicals in Biology and Medicine". The 3rd Edition, Oxford University Press, Oxford.
- Husdan, H. and Rapoport, A. (1968): Estimation of creatinine by Jaffe reaction method. *Clin. Chem.*; **14**: 222-228.
- Jacob, N.J. and Van-Denmark, P.J. (1963): A chemical method for the determination of triglycerides. *Arch. Biochem. Biophys.*; **88**: 250-255.
- Jeong, T.C.; Kim, H.J.; Park, J.I.; Han, C.S.; Park, J.D.; Kim, S.I. and Rah, J.K. (1997): Protective effects of red ginseng saponins against carbon tetrachloride-induced hepatotoxicity in Sprague Dawley rats. *Planta Medica*; **63**(2):136-140.
- Kawak, Y.S.; Kyung, J.S.; Kim, J.S.; Cho, J.Y. and Rhee, M.H. (2010): Antihyperlipidemic effects of red ginseng acidic polysaccharides from Korean red ginseng. *Biol. Pharm. Bull.*; **33**(3): 468-472.

- Khan, N. and Sultana, S. (2004): Abrogation of potassium bromate-induced renal oxidative stress and subsequent cell proliferation response by soy isoflavones in Wistar rats. *Toxicol.*; **201**: 173-184.
- Kim, K. and Kim, H.Y. (2008): Korean red ginseng stimulates insulin release from isolated rat pancreatic islets. *J. Ethnopharmacol.*; **120(2)**: 190-195.
- Kohrle, J.; Jacob, F.; Contempre, B. and Dumont, J. E. (2005): Selenium, the thyroid, and the endocrine system. *Endocrine reviews*; **26**: 944-984.
- Krajcovicova-Kudlackova, M.; Valachovicova, M.; Mislanova, C. and Pribiojova, J. (2012): Antioxidative vitamins and oxidative lipid and DNA damage in relation to nutrition. *Oxid. Antioxid. Med. Sci.*, **1**: 147-151.
- Kurokawa, Y.; Maekawa, A.; Takahashi, M. and Hayashi, Y. (1990): Toxicity and carcinogenicity of potassium bromate, a new renal carcinogen. *Environ. Health Perspect.*; **87**: 309-335.
- Lee, H.U.; Bae, E.A.; Han, M.J. and Kim D.H. (2005): Hepatoprotective effect of 20(S)-ginsenosides Rg3 and its metabolite 20(S)-ginsenoside Rh2 on tert-butyl hydroperoxide-induced liver injury. *Biol. Pharmaceut. Bull.*; **28(10)**: 1992-1994.
- McKenzie, R.C.; Rafferty, T.S. and Beckett, G.J. (1998): Selenium: an essential element for immune function. *Immunol. Today*; **19**: 342-345.
- Ng, T.B. and Yeung, H.W. (1985): Hypoglycemic constituents of *Panax Ginseng*. *Gen. Pharmacol.*; **16 (6)**: 549-552.
- Ohkawa, H.; Ohahi, N. and Jodi, K. (1979): Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Anal. Biochem.*; **95**: 351-358.
- Paglia, D.F. and Valentaine, W.N. (1979): Studies on glutathione and glutathione characterization of erythrocytes glutathione peroxidase. *J. Lab. Clin. Med.*; **70**: 158-169.
- Patton, C. J. and Crouch S.R. (1977): Enzymatic colorimetric method for determination of urea in serum. *Anal. Chem.*; **49**: 464-465.
- Placer, Z.A.; Cushman, L. and Johnson, B. (1966): Estimation of product of lipid peroxidation (malondialdehyde) in biochemical system. *Anal. Biochem.*; **16**: 359-364.
- Pryor, W. A. and Squadrito, G. L. (1995): The chemistry of peroxynitrite: a product from the reaction of nitric oxide with superoxide. *Am. J. Physiol.*; **268(5)**: 699-722.
- Ratliff, C.R. and Hall, F. (1973): A new method for direct colorimetric determination on serum cholesterol. Cited in *Laboratory Manual of Clinical Biochemistry*, Scoot and White Memorial Hospital publication, Texas, USA.
- Rayman, M.P. (2000): The importance of selenium to human health. *Lancet*; **356**: 233-241.
- Reeves, P.G.; Nielson, F.H. and Fahmy, G.C. (1993): Reports of the American Institute of Nutrition, adhoc Willing Committee on Reformulation of the AIN 93 Rodent diet. *J. Nutri.*; **123**: 1939-1951.
- Reuter, S.; Gupta, S.C.; Chaturvedi, M.M. and Aggarwal, B.B. (2010): Oxidative stress, inflammation, and cancer: How they are linked?. *Free Radic. Biol. Med.*; **49(11)**: 1603-1616.
- Rice-Evans, C.A.; Miller, N.J. and Paganga, G. (1996): Structure- antioxidant activity relationships of flavonoids and phenolic acids. *Free Radic. Biol. Med.*; **(20)**: 933-956.
- Snedecor, G.W. and Cochran, W.G. (1986): *Statistical Methods*, The 7th Edition, Iowa State University Press, Ames, USA, Page 90.
- Shin, S.K.; Kwon, J.H.; Jeong, Y.J.; Jeon, S.M.; Choi, J.Y. and Choi, M.S. (2011): Supplementation of cheonggukjang and Korean red ginseng Cheonggukjang combination can improve plasma lipid profile and fasting blood glucose concentration in subjects with impaired fasting glucose. *J. Food Med.*; **14**: 108-113.
- Sinha, K.A. (1972): Colorimetric assay of catalase enzyme. *Anal. Biochem.*; **47**: 328-330.
- Spitz, D.R. and Oberley, L.W. (1989): An assay for superoxide dismutase activity in mammalian tissue homogenates. *Anal. Biochem.*; **179**: 8-18.
- Takaku, T.; Kameda, K.; Matsuura, Y.; Sekiya, K. and Okuda, H. (1990): Studies on insulin-like substances in Korean red ginseng. *Planta Medica*; **56**: 27-30.
- Thomson, C.D. (2004): Assessment of requirements for selenium and adequacy of selenium status: A review. *Eur. J. Clin. Nutri.*; **58**: 391-402.
- Yiming, X.; Kristina, E.; Daniel, W.; Jiayuan, X. and Raymond, F. (2005): Effectiveness of selenium supplements in a low-selenium area of China. *Am. J. Clin. Nutri.*; **81(4)**: 829-834.

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