Effect of Aqueous Extract of Damsissa(*Ambrosia maritima*) on The Biochemical Changes Induced By Potassium Dichromate In Rats

[1*]N. E. Mohamed and [2]R. A. Saber

[1]Biological Applications Department, Nuclear Research Center, Atomic Energy Authority, P.O.13759, Cairo, Egypt
[2]National Organization For Drug Control and Research (NODCAR),P.O.12553 Cairo, Egypt
[*]nelshahat@yahoo.com

Abstract: Chromium is a naturally occurring element found in volcanic dust, in earth crust and is widely distributed in air, water, rocks, soil, plants and animals**.** Humans are occupationally, environmentally, or intrinsically (Surgery implants), exposed to high Cr^{6+} concentrations (8.9 mg/m^3, 20mg/L, 890 mg/kg) respectively. The general population may be exposed to Cr $^{6+}$ compounds through inhalation of ambient air , ingestion of water ,or dermal contact with products that contain chromium (VI) compounds such as pressure treated wood**.** The present study aims to evaluate the antioxidant effect of aqueous extract of Damsissa (Ambrosia maritima) against biochemical changes induced by potassium dichromate in rats. The study was conducted on 48 rats which were classified into four equal groups. Group I : untreated animals (control).Group II: Damsissa treated group: rats were orally supplemented with aqueous extract of damsissa at dose of 100 mg/ kg b.wt. for 14days using stomach tube. Group III: Potassium dichromate treated group, animals injected subcutaneously with potassium dichromate at dose of 10 mg/kg b.wt. for fourteen days , then the half number of the animals sacrificed and the remaining animals left without any treatment for seven days(recovery period).Group IV: Combined treatment group: animals were orally administrated with aqueous extract of damsissa by means of stomach tube at dose of 100 mg/kg b.wt. and injected subcutaneous with potassium dichromate at dose of 10 mg/kg for two weeks and the half number of the animals sacrificed and the remaining animals left without any treatment for one week. Six rats from different groups were sacrificed after 14 days and the rest were left for 7 days as a recovery period. The obtained results revealed significant increase in TBARS concentration which was accompanied with significant decrease in GSH content and CAT activity in renal tissue in treated group with potassium dichromate also, significant increase in urea and creatinine was recorded. The serum levels of sodium significantly increased and the levels of potassium significantly decreased as a consequence to the decrease in aldosterone levels. Calcium and estradiol (E2) levels significantly decreased. However, the levels of phosphorous (P), magnesium (Mg) and parathermone hormone (PTH) were significantly increased in animals injected with potassium dichromate. Consecutive administration of aqueous extract of damsissa with potassium dichromate for 14 days revealed significant improvement in the tested parameters. Also, animals injected with potassium dichromate and left without any treatment for one week as a recovery period showed significant improvement in some of the tested parameters. In conclusion, the results demonstrate the protective role of damsissa against oxidative stress and biochemical changes of potassium dichromate.

[N. E. Mohamed and R. A. Saber. **Effect of Aqueous Extract of Damsissa (*Ambrosia maritima*) on The Biochemical Changes Induced By Potassium Dichromate In Rats.** Journal of American Science 2011;7(3):234-242]. (ISSN: 1545-1003). http://www.americanscience.org.

Key Words: *Ambrosia maritima*, Potassium dichromate, Kidney function , Radioimmunoassay, Oxidative stress .

1. Introduction:

Chromium is a naturally occurring element found in volcanic dust, in earth crust and is widely distributed in air, water, rocks, soil, plants and animals (**Arreola-Mendoza et al.,2006**). The most common forms of chromium in the environment are Cr^0,hexavalent Cr^{6+},or chromate and trivalentCr^{3+},or chromite (**Costa,1997**).Cr^{6+} and Cr^0 are widely used in industrial and chemical processes such as in leather tanning, printing, hair dyes, stainless steel manufacturing, manufacture of pigments, metal finishing (chrome plating),and in wood preservative production (**ATSDR, 2000**). Chromium (VI) compounds also are used in textile dyeing processes, printing inks, drilling mud's water treatment and chemical synthesis **(HSDB,2003**).In some regions, waste disposal of chromium compounds to the environment contributes to increase its presence and potential toxicity(**Armienta-Hernandez and Rodriguez-Castillo,1995).**

Humans are occupationally **(Proctor et al., 2003**), environmentally (**Kerger et al., 2009**) or intrinsically,(Surgery implants, **Keegan et al.,2008**) exposed to high Cr^{6+} concentrations (8.9 mg/m^3,20mg/L,890 mg/kg) respectively. The general population may be exposed to Cr $^{6+}$ compounds through inhalation of ambient air, ingestion of water, or dermal contact with products that contain

chromium (VI) compounds such as pressure treated wood. People who live near industrial facilities that use chromium(VI) compounds or near chromium waste disposal sites have the greatest potential for exposure (**ATSDR,2000**).Chromium was detected in vegetables, fruits ,grains, cereals, eggs, meat, and fish at concentrations between 20 and 520 µg /kg(**ATSDR,2000**). The main daily dietary intake of chromium was estimated to be less than 0.2 to 0.4µg from air 2.0µg from water and 60µg from food specified color additives may contain chromium as chromates (**ATSDR, 2000**).The organs distribution of hexavalent chromium are more widespread with the kidneys, spleen, liver, lungs and bone accumulating significant concentrations of metal. Blood and tissue samples of human may become highly contaminated by the chromium in needles knives, blenders and other instruments (**WHO, 1988**). It is possible that chromium can accumulate in kidneys and heart as elevated levels have been reported in these organs in chromium platters (**WHO, 1988**).

Important issues in the carcinogenic risk assessment of chromium compounds are whether both trivalent and hexavalent chromium compounds. Workers in chromate production plants where the risk of lung cancer is elevated are exposed to both trivalent and hexavalent chromium compounds(**Gibb and Chen,1989).**

Hexavalent chromium is used in a wide range of industries. Cr-VI from chromate industries and atmospheric emissions contribute to the Cr contamination in the environment (**Banu et al.,2008**).Cr^{6+} compounds are highly toxic. They induced dermatotoxicity, immunotoxicity, neurotoxicity, genotoxicity and carcinogenicity, (**Bagchi et al., 2002**). Nephrotoxicity with increased urinary β-2 microglobulin and acute tubular necrosis has been reported in ferrochromate workers exposed acute and chronically to Cr^{6+} (**Wedeen and Qian, 1991).**

Ambrosia maritima L.(Compositae) an annual herbaceous plant widely distributed throughout the Mediterranean region and Africa. It is well known in Egypt under the name of Damsissa. It acts as antispasmodic, diuretic, and useful in bronchial asthma, spasms, and frequent urination (**Ghazanfar, 1994**). It contains important sesquiterpene lactones and flavonoids which showed molluscicidal effect (**Evans, 1996**).

The most active ingredients of this plant are ambrosin and damsin(**Shoeb and El-Eman,1976**). **Alard et al.,(1991)** fed damsissa leaves to rats as a powder or as an alcoholic extract and did not report any toxicity.Damsissa is not toxic to non target organisms (rats,rabbits,algae and daphnia) **Geerts et al.**,(**1992**). Nowadays, its used in some renal tea due to it is proved effect in renal colic and expel renal stons(**Saker et al.,2000**).

In view of the increasing interest in the use of medicinal plants as a natural antioxidant. The present study was planned to evaluate the antioxidant effect of aqueous extract of damsissa (*Ambrosia maritima)* against biochemical changes induced by potassium dichromate in rats.

2. Materials And Methods

2.1.1 Chemicals and plant

Potassium dichromate was purchased from Sigma company. Damsissa plant was obtained from the plant farm of the National Organization For Drug Control and Research, Cairo, Egypt. The other chemicals used were in analytical grade.

2.1.2 Aqueous Extract of Damsissa

Fresh damsissa plants were dried in shade, then crushed dried plants by using of (Micro-Feinula-Culotti) MFC. The aqueous extract of damsissa was prepared by dissolving dried plant in deionized distilled water by continuous stirring at room temperature for 24 h. The extract was filtered, evaporated and dryness under vacuum and the residue was stored at 4ºC until use.

2.2.1 Animals

The study was carried out on 48 female albino rats (130-140 g). Rats were obtained from the animal house of the Nuclear Research Center, Egyptian Atomic Energy Authority, Inshas, Egypt. Animals were kept under normal conditions, standard diet and water *ad libtum*.

2.2.2 Experimental design

The animals were classified into four equal groups. Group I : untreated animals (control). Group II: Damsissa treated group: rats were orally supplemented with aqueous extract of damsissa at dose of 100 mg/ kg b.wt. for 14days orally using gastric tube intubation (**Ahmed and Khater,2001**) .Group III :Potassium dichromate treated group: animals injected subcutaneously with potassium dichromate at dose of 10 mg/kg b.wt. for 2 weeks (**Baggett and Berndt,1986**), then the half number of the animals sacrificed and the remaining animals left without any treatment for one week (recovery period).Group IV:Combined treatment group: animals were orally administrated with aqeous extract of damsissa by gavages using stomach tube at dose of 100 mg/kg b.wt. and injected subcutaneous with potassium dichromate at dose of 10 mg/kg for two weeks and the half number of the animals sacrificed and the remaining left without any treatment for one week(recovery period).

Six rats from different groups were sacrificed after 14 days (2 weeks) and the remaining were left for 7 days which represent the recovery period .Blood samples were collected on plain tube to separate the serum and kept frozen at -20 °C until pending the biochemical assays. Kidney was rapidly excised, washed, dried, weighed and homogenized with phosphate buffer pH7.4 and kept frozen until used for the biochemical assays.

2.2.3 Biochemical assays:

Sera samples were collected to determine, urea, creatinine, sodium, potassium, calcium, phosphorous and magnesium colorimetrically using spectrophotometer (Milton Roy Spectronic 1201) using commercial kits purchased from BioMerieux (France). Aldosterone hormone and estradiol (E2) were determined using radioimmunoassay kit purchased from Immunotech A Beckman Coulter Company France. Serum parathyroid hormone (parathermone) (PTH) level was determined using radioimmunoassay kit purchased from Diagnostic Products Corporation (DPC), Los Angeles, California, USA. The day before sacrifice the rats vaginal smear was done to determine the estrous stage so the estradiol level represent the mean levels of eostrous cycle.Lipid peroxidation in kidney tissue was ascertained by the formation of thiobarbituric acid reactive substance (TBARS) according to the method of **Yoshioka et al.,(1979)**. Reduced glutathione content (GSH) and catalase activity (CAT) were determined according to the method described by **Beutler et al.,** (**1963**) and **Bergmeyer et a**l., (**1987**) in renal tissue.

2.3 Statistical analysis

Results were expressed as mean ±standard error (SE) and differences between the groups were determined by ANOVA (One Way Analysis of Variance) according to **Snedecor and Cochran** (**1982**), followed by Duncan multiple rang test (**Duncan,1955**).

3. Results:

As shown in table(1), demonstrated that administration of aqueous extract of damsissa to rats for 14 days showed that the activity of CAT, the content of GSH and the concentration of TBARS in renal tissue were within normal level as compared with the control group. The obtained results showed that treatment with potassium dichromate induced oxidative stress notified by a significant increase in the level of TBARS associated with a significant($P<0.05$) decrease in GSH content and CAT activity as compared to control values throughout the experimental period. Also, as shown in table (2) a significant($P<0.05$)increase was recorded in serum urea and creatinine. Administration of aqueous extract of damsissa to rats during the experimental period caused a significant ameliorative effect in kidney function. The data in table (3) showed that the rats injected with potassium dichromate exhibited a significant decrease in serum potassium and aldosterone levels accompanied with significant($P<0.05$) increase in serum sodium levels as compared to the control group.

Table (1): Effect of aqueous extract of damsissa on lipid peroxidation (TBARS), reduced glutathione (GSH) content and catalase (CAT) activity in renal tissue in different rats groups.

Parameters	Interval time (days)	Groups (n=6)			
		Control	Damsissa	Potassium dichromate	Damsissa +Potassium dichromate
TBARS µmol/g wet tissue	14	17.04 ± 0.66^{c}	15.05 ± 1.01^{c}	30.37 ± 1.17^{a}	21.21 ± 0.19^{b}
	Recovery	16.71 ± 1.36^{b}	17.72 ± 1.12^{b}	26.50 ± 1.16^{a}	18.02 ± 1.13^{b}
GSH mg/g wet tissue	14	15.21 ± 0.91^{a}	15.27 ± 0.20^{a}	11.49 ± 0.15^{b}	15.53 ± 1.38^{a}
	Recovery	15.87 ± 0.59^{a}	15.74 ± 0.23^{ab}	12.76 ± 0.26^{d}	14.27 ± 0.60^{ac}
CAT U/g wet tissue	14	17.29 ± 0.30^{a}	17.60 ± 0.30^{a}	12.93 ± 0.20^{c}	15.72 ± 0.13^{b}
	Recovery	17.50 ± 0.15^{a}	17.08 ± 0.27^{ab}	14.79 ± 0.55^{c}	16.63 ± 0.28^{b}

Data represented as mean ± SE

Means with different superscripts in the same row are significantly different ($P < 0.05$).

Table (2): Effect of aqueous extract of damsissa on serum urea and creatinine levels in different rats groups.

Parameters	Interval time (days)	Groups (n=6)			
		Control	Damsissa	Potassium dichromate	Damsissa +Potassium dichromate
Urea mg/dl	14	48.31±0.24^{c}	45.51±0.77^{d}	71.20±1.87^{a}	54.59±2.66^{b}
	Recovery	40.87±1.65^{c}	40.08±1.02^{c}	51.33±1.11^{a}	46.35±1.77^{b}
Creatinine mg/ dl	14	0.71±0.01^{c}	0.70±0.02^{c}	0.91±0.04^{a}	0.79±0.03^{b}
	Recovery	0.68±0.03^{c}	0.65±0.02^{c}	0.86±0.01^{a}	0.78±0.03^{b}

Data represented as mean ± SE

Means with different superscripts in the same row are significantly different (P < 0.05).

Table (4) showed significant (P<0.05) decrease in calcium and estradiol(E2) levels in animals injected with potassium dichromate as compared to the corresponding control group. Also, data revealed a significant (P<0.05) increase in phosphorous, magnisum and parathermone hormone in animals treated with potassium dichromate.

The data in Tables(3 and 4) showed significant(P<0.05) ameliorative effect in the serum levels of Na^{+}, K^{+}, aldosterone ,Ca,P,Mg,PTH and E2 in the investigated animals treated with aqueous extract of damsissa and potassium dichromate at the same time. Also, the recovery period of potassium dichromate group revealed significant(P<0.05) improvement of some tested parameters but it was more obvious in animals treated with aqueous extract of damsissa.

Table (3): Effect of aqueous extract of damsissa on serum electrolytes levels and aldosterone level in different rats groups.

Parameters	Interval time (days)	Groups (n=6)			
		Control	Damsissa	Potassium dichromate	Damsissa + Potassium dichromate
Na^{+} mmol/L	14	147.40±0.25^{c}	147.43±3.35^{c}	193.6±2.09^{a}	176.26±1.59^{b}
	Recovery	149.48±1.39^{c}	150.46±2.75^{cb}	176.92±1.59^{a}	156.77±1.60^{b}
K^{+} mmol/L	14	5.82±0.29^{a}	5.87±0.31^{a}	3.69±0.18^{c}	4.70±0.41^{b}
	Recovery	5.91±0.50^{a}	5.71±0.47^{a}	3.80±0.22^{b}	4.95±0.46^{a}
Aldosterone pg/ml	14	297.38±3.75^{a}	289.52±3.61^{a}	235.95±3.90^{c}	270.10±5.99^{b}
	Recovery	286.73±2.94^{a}	293.60±3.78^{a}	272.09±2.57^{b}	283.12±4.21^{a}

Data represented as mean ± SE

Means with different superscripts in the same row are significantly different (P < 0.05).

Table (4): Effect of aqueous extract of damsissa on seum levels of calcium(Ca), phosphorous(P), magnesium (Mg), parathermone hormone (PTH) and estradiol hormone (E2) in different rats groups.

Parameters	Interval time (days)	Groups (n=6)			
		Control	Damsissa	Potassium dichromate	Damsissa +Potassium dichromate
Ca mg/dl	14	7.27±0.28^{a}	6.93±0.52^{ab}	5.30±0.32^{c}	6.23±0.26^{b}
	Recovery	6.83±0.26^{a}	6.89±0.38^{a}	4.47±0.27^{c}	5.83±0.25^{b}
P mg/dl	14	3.14±0.12^{b}	2.97±0.14^{b}	3.80±0.23^{a}	3.29±0.71^{ba}
	Recovery	3.05±0.14^{b}	3.10±0.10^{b}	3.75±0.27^{a}	3.20±0.11^{ba}
Mg mg/dl	14	2.23±0.14^{b}	2.24±0.17^{b}	2.83±0.12^{a}	2.30±0.19^{b}
	Recovery	2.21±0.12^{b}	2.19±0.16^{b}	2.69±0.15^{a}	2.25±0.12^{b}
PTH pg/ml	14	7.89±0.32^{c}	8.07±0.40^{c}	11.37±0.55^{a}	9.19±0.22^{b}
	Recovery	8.29±0.19^{b}	8.18±0.19^{b}	9.68±0.18^{a}	8.73±0.27^{b}
E2 ng/ml	14	17.81±1.07^{ab}	18.78±0.98^{a}	13.32±0.52^{c}	15.70±0.85^{b}
	Recovery	17.90±1.37^{a}	17.75±1.19^{a}	13.90±0.44^{b}	16.41±0.97^{a}

Data represented as mean ± SE

Means with different superscripts in the same row are significantly different (P < 0.05).

4. Discussion

The need for economic, less toxic and more common phytoprotective alternative against environmental toxicity, any xenobiotics and heavy metals induced biological hazards to the living cells sequela directed many researches to test different locally available herbs as a natural protective material.

Reactive oxygen species (ROS) produce a wide variety of toxic effects including DNA damage and lipid peroxidation,and therefore the toxic effects of Cr^{6+} may in part be caused by the production of these species(**Arreola-Mendoza et al., 2006**). However, exposure to chromate has been related to oxidative stress due to Cr^{6+} which is a strong inducer of several chromium reactive intermediaries and free oxygen radicals (**Appenroth et al., 2001 and Bagchi et al., 2002**). They provoke the oxidation of macromolecules like DNA and lipids (**Bagchi et al., 1995**) and kidney (**Bosgelmez and Guvendik, 2004**).

The present results indicated significant increase in TBARS in renal tissue as a consequence to potassium dichromate injection. These results became in agreement with (**Arreola-Mendoza et al., 2009**), who reported that owing to the oxidative properties of Cr^{6+} ,its administration led to a rise of lipids oxidative damage visualized by the increase in renal cortical malondealdehyde(MDA) concentration which was evident on day 2 after treatment with potassium dichromate(15mg/kg b.wt.). These indicate that metal such as chromium undergo redox cycling resulting in the production of reactive oxygen species **(Das,2009**). As a consequence of enhanced lipid peroxidation and altered calcium and sulfhydryl homeostasis (**Das et al, 2006).**

Animals administrated with aqueous extract of damsissa and potassium dichromate together had less oxidative damage than that received potassium dichromate alone. These results suggested that aqueous extract of damsissa protect against the oxidative renal damage caused by Cr^{6+}.So, treatment with aqueous extract of damsissa averted oxidative damage probably through its capacity to quickly and efficiently scavenge lipid peroxyl radicals before they attack membrane lipids. In the present study animals left for 7 days after last dose of injection with potassium dichromate without any treatment served as a recovery period in order to follow up the time required to restore the normal levels of the studied parameters. It was observed that TBARS in recovery group decreased. It proved that the renal tissue became capable to regenerate damage tissue. Thus reduction in the TBARS concentrations might be associated to regeneration of renal tissue. The obtained results became in harmony with **Imai et al.,(1996**), who reported that in a recovering tissue MDA concentration is lower than in a recently injured one.

In biological systems, the soluble forms of Cr^{6+} are absorbed more easily than Cr^{3+} and are reduced to Cr^{3+} via Cr^{5+} by glutathione, ascorbate and hydrogen peroxide (**Aiyar et al., 1991, Stearns et al., 1994**). Once chromium is absorbed, it is distributed in the liver, lung, spleen, kidney, and heart (**Arreola-Mendoza et al.,2006).**

The obtained results recorded significant decrease in GSH content and CAT activity in renal tissue after injection with potassium dichromate. This break down of the GSH and CAT dependent antioxidant defensive system increase the intracellular flux of oxygen free radicals which create an oxidative stress and initiating apoptosis of the cell (**Miesel and Zuber, 1993)**. However, GSH is the most abundant non protein sulfhydryl containing compound in plants and constitutes the largest component of the endogenous thiol buffer (**Holmgren et al., 2005**). So, assessment of GSH in biological samples is essential for evaluation of the redox homeostasis and detoxification status of cells in relation to its protective role against oxidative and free radical mediated cell injury (**Rossi et al.,2005**).GSH has diverse cellular functions in addition to its antioxidant properties including enzymatic conjugation through the glutathione-S- transferase family of proteins and nonenzymatic conjugation to cytotoxic compounds. It is kept in its reduced form by the NADPH dependent enzyme, glutathione disulfide reductase. Moreover,GSH may react with H_2O_2 and lipid peroxides by the action of GSH peroxidase to eliminate the reactive intermediates by reduction of hydroperoxides **(Davis et al.,2001**).

In the present study the decrease in GSH content in renal tissue in rats treated with potassium dichromate might be due to enhanced utilization during detoxification process. Also,catalase acts as a preventive antioxidant plays an important role in protection against the deleterious effects of lipid peroxidation(**Pigeolot et al.,1990**). The depletion of GSH content and catalase activity in renal tissue of rats treated with potassium dichromate may be due to the increased utilization of these antioxidants to counter lipid peroxidation production.

Administrations with aqueous extract of damsissa alleviate the production of lipid peroxidation to become nearly the normal levels in renal tissue which supports the view that the plant under the investigation prevents chromate induced depletion of GSH and catalase activity. Phytochemical analyses on *Ambrosia maritima* extract have identified the presence of some coumarins as scopoletin, umbelliferone and isoscopoletin. In addition, other coumarins like isoprimpipinellin, limettin, esculetin and umbelliprenin were also found **(Khalil et al., 1981**). Also, many of the following compounds were isolated from the crude herb include damsin, ambrosin,neoambrosin, parthenin,

hymenin and other pseudoguinolids (**Picman,1986 and Jakupovic et al.,1987).**

Heavy metals are nephrotoxic xenobiotics,that may lead to acute tubular necrosis (**Wang et al.,1994).** Results of the present study revealed that the increase in the degree of injury in kidney caused by potassium dichromate may lead to a significant increase in the resultant urea and creatinine concentration as well as renal TBARS concentration increased and accompanied with significant reduction in GSH content and catalase activity. This result supported by the results of **DE-Ceaurriz and Ban (1991**) who reported that mice administrated with 80 mg/kg b.wt. potassium dichromate revealed damage to about 40-70 % of the proximal tubules of kidney cause renal failure after 8 hours of administration.Previously renal toxicity of Cr^{6+} has been known for a long time (**Bosgelmez and Guvendik,2004**) and its effect as an inducer of oxidative stress has been explored(**Bagchi et al.,1995).**

The increase in urea and creatinine concentration could be considered as an indicator for the elevation of protein catabolic rates (**Guyton.1991)**as well as the depletion of GSH content in renal tissue which enhance utilization of protein resulting in an increase in urea and creatinine levels. However,Cr^{6+} is accumulated in renal cortex(**Wedeen and Qian,1991**) inducing tubular dysfunction(**Wang et al.,1994**) mainly in the proximal tubule(**Arreola-Mendoza et al.,2006**).The elevation in the serum urea and creatinine may be due to injury in the proximal tubular epithelial cells of kidney and sudden fall in glomerular filtration rates(GFR).However, acute renal damage is induced after envieronmental exposure to chromate Cr^{6+} (**Appenroth et al.,2001**).

Animals administrated with aqueous extract of damsissa concurrently with potassium dichromate showed a significant amelioration of the kidney function presented a restoration in both urea and creatinine concentrations almost near the control levels as well as GSH content, CAT activity and TBARS concentration. This may be attributed to the presence of some phytochemicals compounds which had antioxidant properties (**Ahmed and Khater, 2001**).

As a result of treatment with potassium dichromate the transcular absorption of sodium was diminished and urinary losses would also increase (**Arreola-Mendoza et al.,2009**). The abrupt fall of glomerular filtration rate (GFR) could be associated with cells detachment as a result of losses of cell- cell contacts due to obstruction of tubular lumen and changes in ultra filtration pressure (**Arreola-Mendoza et al., 2009).**

The disturbances in Na^+ and K^+ levels induced by potassium dichromate treatment could be attributed to a kind of stress exerted upon the Na^+-K^+ pump mechanism and intern, leads to membrane permeability imbalance with consequent collapse of calcium homeostasis associated with a decrease in Ca^{2+} level in serum as a result of oxidative stress production as induced in irradiated rats(**Kale and Samul,1987**).The disturbance in Na^+ and K^+ serum levels agitated by potassium dichromate can be elucidated as a kind of stress upon the Na^+ -K^+ pumping mechanism and in turn lead to membrane permeability imbalance.

According to the present finding as illustrated in table (3) the level of aldosterone was significantly decreased under the effect of potassium dichromate treatment. Aldosterone is the principle sodium retaining corticosteroid hormone. It maintains normal fluid balance and circulatory volume. Potassium is also a potent regulator of aldosterone synthesis and its decreased levels decrease aldosterone synthesis where as decreased plasma K^+ levels lower aldosterone synthesis. Because aldosterone promotes Na^+ reabsorbtion by facilitating K^+ and H^+ secretion. This regulatory system is a homeostatic mechanism to maintain normal plasma K^+ level (**West , 1985**).

The kidney function tests seemed to be deteriorated in treated animals with potassium dichromate in the present study, urea and creatinine showed significant increase. However, in the kidney serum calcium is filtered and then completely reabsorbed (**Giovanni et al., 2008**). Renal insufficiency is reflected on increased excretion of calcium with consequent decrease of its serum level.

The obtained results indicated significant increase in parathyroid hormone (PTH) in animals treated with potassium dichromate. The normal calcium level is regulated through three major hormones: parathyroid hormone, thyrocalcitonin and 1,25-dihydroxy vitamin D. The rise of PTH in the present study was attributed to the decline in renal function,calcium absorption efficiency and vitamin D levels(**Allan et al.,2004**).Phosphorous homeostasis is maintained in the kidney by varying the tubular reabsorption of phosphorous. The renal clearance of phosphate is an important regulator of the calcium – phosphate balance in life (**Guyton, 1991**).Several authors reported that the increase of serum phosphorous (P) level is accompanied with hypocalcemia (**Guyton**, **1991**). They attributed these results to the changes in circulating level of parathermone hormone (PTH). These disturbance in Na^+,K^+,Ca, P and Mg may be due to renal tubular defects as a result of Cr^{6+} accumulated in the proximal tubules. **Arreola-Mendoza et al.,(2006)** reported that functional alterations induced by Cr^{6+} were located mostly at the proximal tubules site of action of several xenobiotics including heavy metals.

The results of the present study illustrated that injection with potassium dichromate caused significant decrease in estradiol level (E2).Hexavalent chromium is a reproductive metal toxicant that contraverse the

placental barrier and cause a wide range of fetal effects including ovotoxicity(**Banu et al.,2008**). **Elbetieha and Al-Hamood (1997)** concluded that the ingestion of trivalent and hexavalent chromium compounds by adult male and female mice would cause adverse effects on fertility and reproduction. **Recker et al.,(1996)** observed changes in plasma calcium due to estrogen deficiency and **Uemura et al.,(2000)** found an increase in bone turnover processes as a consequence of estrogen deficiency. In the present work the decrease in calcium is linked to the concomitant decrease in estradiol which maintains calcium level. The administration of aqueous extract of damsissa maintained the levels of calcium, phosphorous and estradiol . However, estrogen exerts beneficial effect by suppression of ROS which in turn stimulate osteoclasts(the cells that reabsorb bone). Thus estrogen might prevent bone loss by enhancing thiol antioxidant defenses in bone through keep the calcium and phosphorous homeostasis balance (**Lean et al., 2003).**

Herbals, as botanical medical treatments have generated a great deal of public controversy in recent years. According to the obtained results administration of aqueous extract of damsissa provide a significant ameliorative effect in renal function and reduce the oxidative stress. The administration of aqueous extract of damsissa revealed significant homeostasis of Na^+,K^+, P,Ca and Mg. Also, recorded normal circulating level of aldosterone, PTH and estradiol hormones. This result revealed that aqueous extract of damsissa has a potential antioxidant effect. However**, Perez et al.,(2004)** reported deleterious renal effects induced byCr^{6+} are partially prevented by antioxidants such as retinoic acid, vitaminC (**Fatima and Mohamood,2007**) and alpha tocopherol (**Arreola-Mendoza et al.,2006**).

In view of the obtained results, it could be concluded that treatment with aqueous extract of damsissa (*Ambrosia maritima*) had the ability to attenuate the possible deleterious effects on renal tissue in populations occupationally or accidentally exposed to chromate Cr^{6+} (potassium dichromate). However, it significantly blunted the increase in lipid peroxidation caused by Cr^{6+}, so it has the potential to enhance endogenous antioxidant status.

Corresponding author
Naglaa El- Shahat Mohamed,
Biological Applications Department, Nuclear Research Center, Atomic Energy Authority, Cairo ,Egypt, P.O.13759.
nelshahat@yahoo.com

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21/2/2011