

Improvement effect of tomato seeds and vitamin C on potassium bromate induced renal injury in rats

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Abstract : Fifty-four adult male of white albino rats (Sprague Dawley Strain) were injected with a single intra-peritoneal dose of potassium bromate at level 125 mg /kg body weight to induce renal injury. Rats classified into non treated positive control group and five treated groups that were tomato seeds powder, tomato seeds extract, vitamin C, tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups. The study was conducted for ten weeks. The results revealed that, the treatment of renal injured rats with tomato seeds powder or extract with or without vitamin C showed improvement of nutritional results as a significant increase in final weight, weight gain and food intake compared to positive control group. The value of Food efficiency ratio (FER) was significantly increased in tomato seeds powder, tomato seeds extract, tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups compared to positive control group. Values of blood hemoglobin (HB), packed cell volume (PCV) and red blood cells; serum high density lipoprotein cholesterol (HDLc), glutathione transferase (GST), catalase & superoxide dismutase (SOD) , and kidney glutathione peroxidase (GPX) & glutathione transferase (GST) were significantly increased in all treated groups compared to positive control group. The values of serum cholesterol, cholesterol/HDLc ratio, triglyceride, low density lipoprotein cholesterol (LDLc), creatinine, uric acid, urea & nitric oxide (NO) and kidney malondialdehyde (MDA) were significantly decreased compared to positive control group. White blood cells was significantly increased in tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups while the value of serum very low density lipoprotein cholesterol (VLDLc) was significantly decreased in tomato seeds powder, tomato seeds extract, tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups compared to positive control group.

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Key wards: Renal injury - Potassium bromate- Tomato seed -Vitamin C-Rats.

1. Introduction

Tomato (*Solanum lycopersicum*.) is one of the most widely cultivated vegetable crops. There is a particular interest in tomato so-called "Mediterranean diet" which has recently been associated with a healthier lifestyle. Tomato products include tomato sauce, tomato ketchup, and tomato paste and tomato juice. These have become the favorites of many people due to their high contents of nutritional components (Persia et al., 2003). Tomatoes are rich sources of antioxidant components such as the carotenoid lycopene, vitamin C, and a range of polyphenols. The potentially protective properties of these antioxidants are of great interest and the consumer has already become aware of their potential importance. Tomatoes can cure diarrhea, gall attack, indigestion and restore liver function (Rozzi 2002 and Abd El-Ghany et al., 2011). Tomato pomace is a mixture of tomato skin, pulp and seeds that remain after the processing of tomato. This by product remains from squeeze of tomato is rich in protein, energy and crude fiber. Tomato seed is the major by-product of the tomato paste manufacturing industry and is a potential raw material for producing

alternative fuels. Tomato paste manufacturing units generate 7.0–7.5% solid waste and 71–72% of this waste is pomace, tomato seeds by-product accounts for approximately 10% of the fruit and 60% of the total tomato industry waste (Sogi et al., 2005). A naturally occurring compound found in the seeds of ordinary tomatoes has been discovered to have a major beneficial effect on long term health and blood circulation. The tomato seed compound does not appear to have any known side effects which may be a major advantage in helping people to improve the health of their blood stream and reduce the risk of heart attack and stroke (del Valle, et al., 2007).

Vitamin C is not produced in the body, so it needs to be consumed through food. Vitamin C is good for gums, bones and blood vessels and also stimulates the bodies' immune system, fights infections, promotes wound healing and helps iron absorption. Vitamin C is an important antioxidant and helps protect against cancers, heart diseases and stress. It is part of the cellular chemistry that provides energy, essential for sperm production, for making collagen, involved in the building and health of

cartilage, joints, skins and blood vessels (Champe and Harvey, 1994).

There is a need for studying the health beneficial effect of tomato seeds separately or with vitamin C in improving renal function in experimental rats.

2. Materials and Methods

A – Materials:

Fifty-four adult male of white albino rats (Wister Strain) weighing 102 ± 7 g, were obtained from experimental animals center in Medicine collage of King Saud University in Riyadh. Tomato fruits samples were obtained from Best Factory for food industry in Egypt. The basal diet was prepared according to NRC (1995) which composed of casein (200g/kg), corn starch (497g/kg), sucrose (100g/kg), cellulose (30 g/kg), corn oil (50g/kg), mineral mixture (100g/kg), vitamins mixture (20g/kg) and DL-methionine (3g/kg). Both potassium bromate ($KBrO_3$) and vitamin C were purchased from Somatco Co., in Riyadh. Vitamin C was administered by stomach tube in dose 5 g/100g rats.

B- Methods

A mixture of tomato seeds and skins was obtained as the byproduct of whole tomato processing. Seeds were separated from the skin by water floatation wherein seeds sunk to the bottom and skin floated. The seeds were collected. The seeds were washed with tape water several times, and dried in air oven at $50^\circ C$ and grinded in blender, then the powder packaged in polyethylene bags and kept until use. Tomato seeds powder was added in basal diet as 10 % in substitution of fiber. To prepare tomato methanol extract, 100 gram of tomato powdered was added to 1000 ml of 70% methanol (v/v) at room temperature for 20 hours with slowly rotated during this time. After filtration, ethanol was evaporated at low pressure at $30^\circ C$ and was immediately administered to rats at dose 500 mg/kg body weight by stomach tube (WHO 1983).

Rats were kept under observation for seven days before experiment and fed on basal diet and water ad libitum for adaptation. Rats were injected with a single intra-peritoneal dose of potassium bromate at level 125 mg /kg body weight to induce renal injury (Kahan and Sultana 2004). Rats classified into non treated positive control group and five treated groups that were tomato seeds powder, tomato seeds extract, vitamin C, tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups. The study was assigned for ten weeks.

The food intake was calculated daily and the body weight gain was recorded weekly. Food efficiency ratio (FER) was determined by Chapman et al., (1950) as following: $FER = \text{weight gain (g)} / \text{food intake (g)}$. At the end of experiment, the rats were anesthetized, blood sample were collected in clean centrifuge tubes. Blood hemoglobin (HB), packed cell volume (PCV) and red and white blood cells were estimated according to Drabkin (1949) and Mc Inory, (1954), Carleton (1976), respectively.

Serum cholesterol, triglyceride, and high density lipoprotein cholesterol (HDLc) were estimated according to Allain et al., (1974), Scheletter and Nussel (1975) and Kostener (1977), respectively. In addition, creatinine, urea and uric acid were estimated according to Bonsens and Tausky, (1984), Kanter (1975) and Fossati et al., (1980), respectively. Serum glutathione transferase (GST), catalase, nitric oxide (NO) and superoxide dismutase enzymes (SOD) were estimated according to Habig (1974), Claiborne (1985), Green et al., (1981) and Beuchamp and Fridovich, (1971), respectively. Kidney glutathione peroxidase (GPX), glutathione transferase (GST), and malondialdehyde (MDA) were determined according to Weiss et al. (1980), Habig et al., (1974) and Draper et al., (1993), respectively. Very low density lipoprotein (VLDL c) and low density lipoprotein cholesterol were calculated according Friedewald (1972) and Fruchart (1982) as following: $VLDL\ c = (TG/5)$, $LDL\text{-}c = (\text{Total cholesterol} - VLDL\text{-}c - HDL\text{-}c)$ while athrogenic index (cholesterol /HDL-c ratio) was calculated according to Castelli and levitar (1977). The biochemical analyses were occurred in laboratory of department of Nutrition and Food Science, King Saud University in Saud Arabia.

C-Statistical analysis

All the obtained data were statistically analyzed by SPSS computer soft ware. The calculated occurred by analysis of variance ANOVA and follow up test LSD (Artimage and Berry 1987).

3. Results

Table (1) showed that, the treatment of renal injured rats with tomato seeds powder or extract with or without vitamin C showed improvement of nutritional results. All treated groups showed a significant increase in final weight, weight gain and food intake at $p < 0.01$ & 0.001 compared to positive control group. The value of Food efficiency ratio (FER) was significantly increased in tomato seeds powder, tomato seeds extract, tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups compared to positive control group.

Table (2) showed that values of hemoglobin (HB), packed cell volume (PCV) and red blood cells were significantly increased in all treated groups at $p < 0.05$ & 0.01 compared to positive control group. The value of white blood cells was significantly increased in tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups at $p < 0.01$ compared to positive control group.

Data in table (3) represented that the value of serum cholesterol was significantly decreased at $p < 0.01$ & 0.001 but the value of serum high density lipoprotein cholesterol (HDLc) was significantly increased at $p < 0.01$ in all treated rat groups compared to positive control group. The value of atherogenic index (cholesterol/HDLc ratio) was significantly decreased at $p < 0.05$ in treated groups with tomato seeds powder or extract with or without vitamin C compared to positive control group.

Data in table (4) represented that the value of serum triglyceride and low density lipoprotein cholesterol (LDLc) was significantly decreased at $p < 0.05$, 0.01 & 0.001 compared to positive control group. The value of serum very low density lipoprotein cholesterol (VLDLc) was significantly decreased at $p < 0.05$ in tomato seeds powder and tomato seeds extract groups and at $p < 0.01$ in tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups compared to positive control group.

It was noticed also from table (5) that values of serum creatinine, and uric acid were significantly decreased at $p < 0.05$ and urea at $p < 0.05$ & 0.01 in tomato seeds powder, tomato seeds extract, vitamin C, tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups compared to positive control group.

Data in table (6) presented that serum glutathione transferase (GST), catalase, and superoxide dismutase enzymes (SOD) were significantly increased at $p < 0.01$ & 0.001 but nitric oxide (NO) was significantly decreased at $p < 0.01$ & 0.001 in treated groups that were tomato seeds powder, tomato seeds extract, vitamin C, tomato seeds powder with vitamin C and tomato seeds extract with vitamin C groups compared to positive control group.

Data in table (7) presented that the value of kidney malondialdehyde (MDA) was significantly decreased ($p < 0.05$, 0.01 & 0.001) but the value of kidney glutathione peroxidase (GPX) was significantly increased at $p < 0.01$ & 0.001 and glutathione transferase (GST) was significantly increased at $p < 0.05$, 0.01 & 0.001 compared to positive control group.

4. Discussion

Potassium bromate (KBrO₃) is an oxidizing agent that has been used as a food additive, mainly in the bread-making process. KBrO₃ is carcinogenic in rats and nephrotoxic in both man and experimental animals when given orally. Glutathione and cysteine degrade KBrO₃ in vitro; in turn, the KBrO₃ has inhibitory effects on inducing lipid peroxidation in the rat kidney. Active oxygen radicals generated from KBrO₃ were implicated in its toxic and carcinogenic effects, especially because KBrO₃ produced 8-hydroxydeoxyguanosine in the rat kidney (Kurokawa et al., 1990 and Geter, et al., 2006).

The improvement of our nutritional results may refer to large number of nutrients of tomato seeds. Tomato seeds are believed to be high in carbohydrates and protein, containing nearly all of the essential amino acids. Also, contain a high amount of oil, nearly two thirds of is unsaturated fatty acids. Tomato seeds are rich in minerals such as calcium, magnesium, potassium and some zinc. Tomato seed oil has high antioxidant content (Knoblich et al., 2005 and Denek and Can 2006). Tomato seeds may be limited in energy due to the high fiber content. The administration of tomato seed oil can lower serum total cholesterol, triglyceride and low-density lipoprotein cholesterol levels (Persia et al., 2003 and Li et al., 2007).

It has been reported that tomato seed extracts contain phenolic compounds whose antioxidant activity is well known. The total content of phenolics in 100 g of dry matter ranged from 70 mg in tomato seeds. The skin and seed fractions of tomato, together, contributed 53% of the total phenolics, 52% of the flavonoids, 48% of the total lycopene, 43% of the total ascorbic acid and 52% of the total antioxidant activity present in whole tomatoes. Antioxidant substances in tomato seeds can be helpful in preventing the damage caused by free radicals to body tissues leading to premature aging and many chronic degenerative diseases (Toor 2005 and Ramandeep and Geoffrey 2005). The gel that surrounds [tomato seeds](#) improves blood flow, with improvements evident as soon as three hours after ingesting it because of containing compound or mixture of substances that can prevent blood clotting, so efficacious against stroke and heart disease (Colleen 2009). Iron and vitamin C found in tomatoes promotes the synthesis of hemoglobin and the formation of new red cells, thereby helping to prevent or treat different types of anemia (Harish and Sathishkumar 2011).

It is well known that vitamin C acts as an antioxidant by protecting the body against oxidative stress and helps protect the body from toxins and

chemical pollutants. Vitamin C has an impact on cardiovascular disease, hypertension, chronic inflammatory diseases, and diabetes. It is also a cofactor in at least eight enzymatic reactions and performs numerous physiological functions in the human body including the synthesis of collagen, carnitine, and neurotransmitters; the synthesis and catabolism of tyrosine; and the metabolism of microsome (Padayatty et al., 2003 and Gropper et al., 2004). Vitamin C acts as a reducing agent, cholesterol and work to lower the accumulation of cholesterol in the cell wall. HDLc helps to reduce the risk of heart disease by scavenging cholesterol. Vitamin C stimulates an enzyme that regulates the conversion of cholesterol into bile acids, which are then eliminated from the body in the feces (Naidu 2003).

It is concluded that discarding tomato seeds during home cooking or commercial processing can result in significant losses of antioxidants and

donating electrons and preventing oxidation to keep iron and copper atoms in their reduced states. Vitamin C may be useful in lowering serum uric acid levels, resulting in a correspondingly lower incidence of gout (Naidu 2003). Vitamin C represents one of the most prominent antioxidants both in plasma as well as intracellularly, exerting beneficial effects by an inhibition of lipid peroxidation and by reducing endothelial dysfunction (Deicher and Horl 2003). Vitamin C may increase the beneficial HDLc consumption of tomato seeds with vitamin C have ability to improve healthy status of kidney which exposed to oxidative stress by potassium bromate.

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

Groups	Control (+ve)	Tomato seeds powder	Tomato seeds extract	Vitamin C	Tomato seeds powder +Vitamin C	Tomato seeds extract + Vitamin C
Initial	102.36±	104.55±	103.25±	104.77±	105.22±	102.96±
Weight(g)	3.61 ^a	3.22 ^a	3.11 ^a	4.11 ^a	4.21 ^a	3.67 ^a
Final	157.97±	196.69±	198.86±	182.18±	203.43±	200.57±
Weight(g)	5.11 ^c	3.99 ^{**}	4.27 ^{***}	4.11 ^{b**}	6.77 ^{***}	7.25 ^{***}
Weight gain (g)	55.61±	92.14±	95.61±	77.41±	98.21±	97.61±
Food intake(g/w)	5.21 ^c	9.14 ^{***}	8.13 ^{***}	7.22 ^{b**}	9.12 ^{***}	9.71 ^{***}
FER	12.11±	15.12±	15.05±	14.59±	15.41±	15.12±
	1.20 ^b	1.51 ^{a**}	1.35 ^{a**}	1.21 ^{a**}	1.60 ^{a**}	1.71 ^{a**}
	0.071±	0.102±	0.101±	0.081±	0.103±	0.102±
	0.002 ^b	0.003 ^{a**}	0.001 ^{a**}	0.002 ^b	0.001 ^{a**}	0.004 ^{a**}

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 HG, PCV, RBCs and WBCs of the experimental rat groups

Groups	Control (+ve)	Tomato seeds powder	Tomato seeds extract	Vitamin C	Tomato seeds powder +Vitamin C	Tomato seeds extract +Vitamin C
HG (g/dl)	10.11±	12.99±	13.71±	13.21±	13.11±	13.25±
PCV %	1.25 ^b	1.88 ^{a**}	1.55 ^{a**}	1.35 ^{a**}	1.41 ^{a**}	1.25 ^{a**}
RBCs (x106/ µl)	30.21±	36.29±	38.61±	35.61±	37.96±	37.88±
WBCs (x106/ µl)	3.11 ^b	3.61 ^{a*}	3.61 ^{a**}	4.11 ^{a*}	3.65 ^{a*}	3.21 ^{a*}
	2.90±	3.66±	3.67±	3.96±	4.30±	4.55±
	0.77 ^b	0.91 ^{a**}	0.87 ^{a*}	0.82 ^{a*}	1.01 ^{a**}	1.11 ^{a**}
	5.25±	6.88±	7.21±	7.11±	8.11±	9.36±
	0.94 ^b	1.21 ^{ab}	1.25 ^{ab}	1.31 ^{ab}	1.12 ^{a**}	1.98 ^{a**}

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): Serum cholesterol, HDLc and cholesterol/ HDLc ratio of the experimental rat groups

Groups	Control (+ve)	Tomato seeds powder	Tomato seeds extract	Vitamin C	Tomato seeds powder +Vitamin C	Tomato seeds extract +Vitamin C
Cholesterol (mg/g)	196.14± 13.14 ^a	137.21± 11.21 ^{b**}	120.14± 12.17 ^{bc**}	149.21± 11.81 ^{b**}	122.14± 15.14 ^{c***}	117.81± 13.61 ^{c***}
HDLc (mg/g)	25.31± 2.41 ^c	30.21± 3.61 ^{ab**}	33.21± 4.11 ^{a**}	31.41± 3.21 ^{a**}	31.14± 3.22 ^{a**}	35.21± 3.41 ^{a***}
Cholesterol / HDLc	7.74± 1.31 ^a	4.54± 0.24 ^{b*}	3.61± 0.33 ^{b*}	4.75± 0.43 ^{b*}	3.92± 0.53 ^{b*}	3.34± 0.42 ^{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 (4): Serum triglyceride, LDLc and VLDLc of the experimental rat groups

Groups	Control (+ve)	Tomato Seeds powder	Tomato Seeds extract	Vitamin C	Tomato seeds powder +Vitamin C	Tomato seeds extract +Vitamin C
Triglyceride (mg/g)	112.21± 14.12 ^a	91.14± 9.43 ^{b**}	87.21± 9.35 ^{b*}	98.14± 10.11 ^{b**}	82.14± 9.21 ^{bc*}	77.25± 8.33 ^{c**}
LDLc (mg/g)	148.38± 12.26 ^a	88.78± 8.71 ^{bc*}	69.49± 6.21 ^{d**}	98.18± 9.21 ^{b**}	74.58± 8.14 ^{d**}	67.15± 7.31 ^{d***}
VLDLc (mg/dl)	22.44± 2.33 ^a	18.22± 1.71 ^{b*}	17.44± 1.65 ^{b*}	19.62± 1.24 ^{ab}	16.42± 1.33 ^{bc**}	15.45± 1.37 ^{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 (5): Serum creatinine, urea and uric acid of the experimental rat groups

Groups	Control (+ve)	Tomato seeds powder	Tomato seeds extract	Vitamin C	Tomato seeds powder +Vitamin C	Tomato seeds extract +Vitamin C
Creatinine (mg/dl)	1.87± 0.33 ^a	0.89± 0.02 ^{b*}	0.87± 0.11 ^{b*}	1.21± 0.43 ^{b*}	0.78± 0.12 ^{b*}	0.75± 0.18 ^{b*}
Urea (μ /mg)	59.16± 6.24 ^a	43.21± 4.35 ^{b*}	40.21± 4.81 ^{b*}	45.61± 5.18 ^{b*}	41.31± 5.14 ^{b*}	39.61± 4.45 ^{b**}
uric acid (mg/dl)	4.77± 1.11 ^a	2.71± 0.88 ^{b*}	3.02± 0.87 ^{b*}	2.71± 0.33 ^{b*}	2.51± 0.32 ^{b*}	2.11± 0.25 ^{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): Serum GST, catalase, NO and SOD of the experimental rat groups

Groups	Control (+ve)	Tomato seeds powder	Tomato seeds extract	Vitamin C	Tomato seeds powder +Vitamin C	Tomato seeds extract +Vitamin C
GST (μ /l)	95.11± 9.14 ^c	124.11± 12.25 ^{b**}	151.21± 15.14 ^{ab**}	131.21± 13.24 ^{b**}	161.41± 16.28 ^{a***}	181.31± 20.11 ^{a***}
Catalase (μ /mg))	91.14± 10.33 ^c	178.36± 18.77 ^{b**}	211.14± 22.14 ^{a***}	188.36± 20.76 ^{b**}	214.31± 22.66 ^{a***}	250.77± 25.28 ^{a***}
NO (μ /ml)	14.33± 2.68 ^a	7.21± 1.13 ^{b**}	5.14± 1.21 ^{b**}	6.81± 1.01 ^{b**}	5.11± 1.21 ^{b**}	3.67± 0.88 ^{c***}
SOD (μ /mg)	22.61± 2.61 ^c	45.21± 5.33 ^{d**}	65.11± 6.21 ^{b***}	55.31± 6.11 ^{c***}	70.11± 7.31 ^{b***}	82.11± 9.24 ^{a***}

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 (7): Kidney MDA, GPX and GST of the experimental rat groups

Groups	Control (+ve)	Tomato seeds powder	Tomato seeds extract	Vitamin C	Tomato seeds powder +Vitamin C	Tomato seeds extract +Vitamin C
Variables						
MDA (mmol/g)	18.67±	11.60±	9.11±	10.31±	8.25±	7.11±
GPX (µ /mg)	1.66 ^a	1.81 ^{b*}	1.30 ^{b*}	1.21 ^{b*}	0.95 ^{bc**}	0.68 ^{c**}
GST (µ /mg)	35.77±	85.14±	92.61±	87.41±	98.61±	112.31±
	4.33 ^d	5.88 ^{c***}	9.41 ^{bc**}	8.77 ^{c**}	10.11 ^{a***}	12.45 ^{a***}
	2.01±	3.99±	4.86±	4.71±	4.82±	5.11±
	0.15 ^c	0.55 ^{b*}	0.88 ^{a**}	0.83 ^{a**}	0.66 ^{a**}	0.54 ^{a***}

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.

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