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Dried Fruit Extract of Sumac (*Rhus coriaria* L) Protects Albino Rats from Adverse Effects of Whole Body γ-Radiation

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THE ANTIOXIDANT effect of Sumac; *Rhus coriaria L.* against whole body gamma-irradiation-induced oxidative damage in lung and liver tissues was investigated in albino rats. To achieve the ultimate goal of this study, 48 adult rats were randomly divided into 4 groups of 12 animals each. Group I: Control group. Group II: Irradiated with a single dose of 5Gy γ-rays. Group III: Fed with sumac orally (300 mg/ kg body wt/ day) for 10 days. Group IV: Fed sumac (300 mg/ kg body wt) for 3 days pre-irradiation and 7 days after-radiation (5 Gy). The rats were sacrificed 1 and 7 days after a single exposure to γ-rays. The animals exposed to gamma radiation recorded significant increase in malondialdehyde (MDA) and total nitrate oxide (NO) levels in both lung and liver tissues. Also the results revealed, significant decrease in the activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GSHPx) and the level of reduced glutathione (GSH), in lung and liver tissues. Moreover, a significant increase in plasma glucose accompanied with a significant decrease in insulin level was observed in irradiated rats. Administration of sumac for 10 days to rats prior and post gamma irradiation improved the tested parameters except glucose. In conclusion, data obtained from this study indicated that sumac could increase the antioxidant defence mechanism in rat and there by protects the animals from radiation-induced organs toxicity but it may increase the blood sugar, therefore in diabetic patient be considered.
Keywords: Sumac extract, gamma rays, lung, liver, rats.

Sumac; (*Rhus coriaria* L., family Anacardiaceae) is the common name for a genus Rhus that contains over 250 individual species of flowering. The fruit extracts of sumac have been reported to contain high levels of polyphenols such as gallic acid, anthocyanins and hydrolysable tannins (Kosar *et al.*, 2007).

Sumac extracts possess strong antimicrobial and antioxidant activities (Candan and Sokmen, 2004, Fazeli *et al*., 2007). And also the fruit is rich in oleic and linoleic acids, vitamins as well as minerals (Kossah *et al.*, 2009). These substances have gained interest because they may reduce the risk of chronic diseases reinforcing the defences against free radical species. Ozcan (2003) published that sumac extract is promising as a source of natural antioxidant. The methanolic extracts of *Rhus retinorrhaea* showed a remarkable radical scavenging effect even at low concentrations (Mothana *et al.*, 2009). Ercan and Ekrem (2010) found that water extracts of sumac have effective antioxidant and radical scavenging activities as compared to ethanol extracts.

Exposure to ionizing radiation leads to the generation of extra reactive oxygen species and free radicals which attack sensitive enzymes, constitutive proteins, DNA and membrane lipids (Blatter and Herrlich, 2004). Evidence for oxidative injury is proved from measurements of biochemical markers of lipid peroxidation and protein oxidation. Lipid peroxidation is believed to be an important cause of destruction and damage to cell membranes and has been shown to be a contributing factor to the development of oxygen radicals-mediated tissue damage.

The majority of plants and herbs contain polyphenols has scavenging capacity for radiation-induced free radicals and elevation of cellular antioxidants by plants and herbs in irradiated systems could be leading mechanisms for radioprotection. The polyphenols present in the plants and herbs may up regulate messenger-RNAs (mRNAs) of antioxidant enzymes such as CAT, GSHPx, SOD and thus may counteract the oxidative stress-induced by ionizing radiations (Ganesh, 2007).

The aim of the present study was to examine the radio protective effects of sumac against oxidative damage and organ injury induced by ionizing radiation.

Material and Methods

Administration of sumac

Sumac purchased from local Egyptian herbal market. Hot water extract was prepared as described previously (Ghaleb *et al*., 2006). 30 g of dried powdered plant materials were extracted with hot water; the extract was filtered

through Whatman No. 2 filter paper under suction. Extract was concentrated to dryness in vacuum. Then, 100 mg of the dry residue was dissolved in 1 ml of sterile distilled water.

Animals

Male Albino rats with an average wt of 100-120 g were obtained from the Holding Company for Biological Products and Vaccines, Cairo, Egypt. The animals were kept under good ventilation at a temperature of 22± 3^{o}C, 60% humidity, suitable illumination conditions (light/ dark cycle) and allowed standard pellet diet and fresh water *ad libitum*.

Irradiation

Irradiation was performed through the use of a Canadian Gamma Cell-40 (^{137}Cs) at the NCRRT, Cairo, Egypt. The dose rate was 0.6 Gy/ min**.**

Animals were divided into 4 groups (n= 12) as follows: Group I: Control (Normal saline). Group II: Irradiated animals were subjected to a single dose of whole body γ-rays (5Gy). Group III: Animals were received sumac extract (300 mg/ kg body wt), orally. Group VI: Animals were received sumac extract orally (300 mg/ kg body wt/ day), orally for 3 days pre γ-irradiation and 7 days after radiation (5 Gy).

Blood collection and tissue sampling

Animals were sacrificed on the 1st and 7th day after the γ-rays dose. Blood samples were collected by heart puncture. Liver and lung were quickly removed, rinsed thoroughly from blood in isotonic saline, blotted dry and weighted then homogenized in saline solution. The homogenate was centrifuged at 3000 rpm for 15 min and the supernatant was used for biochemical analysis.

Biochemical study

Lipid peroxidation was determined as MDA as described by Ohkhawa *et al.* (1979). NO concentration was measured by the method of Ignarro *et al.* (1987). CAT, SOD and GSHPx activities were determined according to the methods of Johansson and Borg (1988), Minami and Yoshikawa (1979) and Paglia and Valentine (1967), respectively. The content of GSH was determined

according to the method of Beutler *et al.* (1963). Blood glucose level was measured by enzymatic colorimetric method as described by Trinder (1969). Insulin hormone was determined by radioimmunoassay kit according to Starr *et al.* (1978).

Statistical analysis

The obtained results were subjected to statistical analysis using the standard analysis of variance as outlined by Snedecor and Cochran (1989).

Results

Oral administration of sumac (300mg/ kg body wt) for 10 days does not alter significantly most of the measured tissue parameters Table 1-6.

TABLE 1. Concentration of MDA in liver and lung tissues of different rats groups.

Investigated tissues		Groups			
		Control	Sumac	Irradiated	Sumac+ irradiated
Liver nmol/ g tissue	**1**	201± 3.1[c]	199± 3.3[c]	290± 5.3[a,b,d]	230± 6.5[c]
	7	198± 2.9[c]	195± 3.2[c]	285± 6.4[a,b,d]	223± 5.9[c]
Lung nmol/ g tissue	**1**	201± 9.1[c]	202± 7.3[c]	293± 8.1[a,b,d]	221± 10.3[c]
	7	208±8.3[c]	207± 6.4[c]	298± 10.1[a,b,d]	229±11.5[c]

Each value represents the mean of 5 observations± S.E.
a-significant difference compared to control.
b-significant difference compared to sumac.
c-significant difference compared to radiation.
d-significant difference compared to sumac+ radiation.

In irradiated rats, exposure to single dose whole body gamma irradiation (5Gy) resulted in significant increases in MDA and NO level and significant decrease in GSH content in liver and lung tissues when compared to the corresponding values in control rats.

TABLE 2. Concentration of NO in liver and lung tissues of different rats groups.

Investigated tissues		Groups			
		Control	Sumac	Irradiated	Sumac+ irradiated
Liver nmol/ g tissue	**1**	51.3± 1.3 [c]	51.5± 0.9[c]	63.9± 1.1[a,b,d]	54.5± 0.71[c]
	7	52.1± 1.9[c]	51.9± 0.9[c]	61.3± 0.8[a,b,d]	53.9± 1.1[c]
Lung nmol/ g tissue	**1**	1.5± 0.6[c]	1.53± 0.7[c]	2.7± 0.39[a,b,d]	1.63± 0.4[c]
	7	1.55± 0.3[c]	1.59± 0.75[c]	2.9± 0.46[a,b,d]	1.17± 0.7[c]

Legend as in Table 1.

Administration of sumac before and after exposure to single dose whole body gamma rays induce significant amelioration in levels of MDA , NO and GSH contents at the 1st and 7th / days in liver and lung tissues (Table 1-3).

TABLE 3. Concentration of GSH in liver and lung tissues of different rats groups.

Investigated tissues		Groups			
		Control	Sumac	Irradiated	Sumac+ irradiated
Liver nmol/ g tissue	**1**	25.1± 2.1^{c,d}	25.4± 2.3^{c,d}	17.5± 1.8^{a,b,d}	21.3± 1.7^{abc}
	7	23.5± 1.9^{cd}	24.1± 2.5^{cd}	15.3± 1.5^{abd}	20.19 ±1.8^{abc}
Lung nmol/ g tissue	**1**	19.3± 1.6^{c}	20.6± 2.2^{c}	10.1± 1.6^{abd}	17.1± 1.1^{c}
	7	19.6± 1.7^{c}	19.1± 1.3^{c}	10.3± 1.9^{abd}	16.7± 1.8^{c}

Legend as in Table 1.

In the present study, the activities of CAT, SOD and GSHPx were significantly decreased in irradiated rats group on the 1st and 7th days in liver and lung tissues when compared to control rats (Table 4-6). In addition, significant increase in the activities of CAT, SOD and GSHPx were observed in tissues of rats administrated sumac prior and post irradiation as compared to irradiated rats.

TABLE 4. Effect of sumac extract treatment on CAT activity in liver and lung of irradiated rats after 1 and 7 days.

Investigated tissues		Groups			
		Control	Sumac	Irradiated	Sumac+ irradiated
Liver nmol/ g tissue	**1**	28.5± 0.91^{cd}	29.4± 0.83^{cd}	13.37± 1.5^{ab}	15.3± 0.9^{ab}
	7	29.8± 1.01^{cd}	29.9± 0.79^{cd}	14.1± 1.2^{ab}	19.1± 0.81^{ab}
Lung nmol/ g tissue	**1**	19.1± 0.9^{c}	19.0± 0.89^{c}	13.5± 0.29^{abd}	16.3± 0.51^{c}
	7	18.3± 0.53^{c}	19.3± 0.7^{c}	14.7± 1.01^{abd}	16.0± 0.6^{c}

Legend as in Table 1.

TABLE 5. Effect of sumac extract treatment on SOD activity in liver and lung of irradiated rats after 1 and 7 days.

Investigated tissues		Groups			
		Control	Sumac	Irradiated	Sumac+ irradiated
Liver nmol/ g tissue	**1**	27.9± 3.1^{cd}	27.5± 2.4^{cd}	18.8± 1.9^{ab}	22.5± 1.5^{ab}
	7	28.5± 3.5^{cd}	28.3± 2.8^{cd}	19.5± 2.1^{ab}	22.1± 2.3^{ab}
Lung nmol/ g tissue	**1**	0.91± 0.2^{c}	0.87± 0.3^{c}	0.43± 0.3^{abd}	0.79± 0.7^{c}
	7	0.89± 0.6^{c}	0.85± 0.4^{c}	0.51± 0.5^{abd}	0.81± 0.6^{c}

Legend as in Table 1.

Table 7. shows the level of plasma glucose and insulin of different experimental groups. The irradiated rats showed a significant increase in the level of glucose with decrease in level of insulin. Oral administration of sumac showed increase in level of plasma glucose and decrease in insulin.

TABLE 6. Effect of sumac extract treatment on GSH-PX activity in liver and lung of irradiated rats after 1 and 7 days.

Investigated tissues		Groups			
		Control	Sumac	Irradiated	Sumac+ irradiated
Liver nmol/ g tissue	**1**	30.1± 2.3^{cd}	32.1± 3.1^{cd}	18.9± 0.9^{ab}	27.1± 2.3^{ab}
	7	32.3± 2.5^{cd}	33.0± 4.2^{cd}	17.5± 0.7^{ab}	28.2± 3.1^{ab}
Lung nmol/ g tissue	**1**	82.1± 2.3^{cd}	82.0± 1.9^{cd}	30.9± 3.1^{abd}	49.2± 2.1^{abc}
	7	82.9± 2.5^{cd}	82.3± 2.1^{cd}	32.1± 2.01^{abd}	51.5± 1.9^{abc}

Legend as in Table 1.

TABLE 7. Effect of sumac extract treatment on plasma glucose and insulin in different groups.

Investigated tissues		Groups			
		Control	Sumac	Irradiated	Sumac+ irradiated
Plasma glucose mg/ dl	**1**	126.5± 4.1^{cbd}	160.9± 3.5^{ac}	193.1± 3.9^{ab}	165.3± 2.9^{ab}
	7	129.1± 5.1^{cbd}	167.3± 4.5^{a}	190.3± 4.3^{a}	170.3± 4.5^{a}
Insulin mg/ dl	**1**	3.8± 0.9^{c}	2.9± 1.7^{ac}	1.3± 1.6^{abd}	2.5± 1.5^{ac}
	7	3.9± 1.1^{c}	2.5± 1.3^{ac}	1.1± 1.2^{abd}	2.1± 1.3^{ac}

Legend as in Table 1.

Discussion

Radiation exposure has been reported to be associated with increased disruption of membrane lipids leading to subsequent formation of peroxide radicals (Rajapakse *et al.*, 2007).

The present study demonstrates that whole-body irradiation in rats causes tissue damage in the liver and lung as assessed by decrease antioxidant enzyme activities, and increased lipid peroxidation and NO levels. Insufficient levels of antioxidants to scavenge peroxy-radicals during radiation could have contributed to the elevated level of MDA in irradiated rats (Manda *et al.*, 2007).

Some studies have reported that NO is an important mediator of radiation-induced acute tissue damage (Tsuji *et al.*, 2000). NO has been shown to have a cytotoxic function and the toxicity of NO is due to both NO itself and NO derived reactive oxidants (Beckman and Koppenol, 1996). Activated macrophages produce both NO and $ONOO^-$. Under conditions where the superoxide anion (O_2^-) is generated, NO is rapidly consumed to produce the highly reactive $ONOO^-$, a potent oxidizing agent known to initiate lipid peroxidation of biological membranes, hydroxylation and nitration of aromatic amino acid residues and sulfhydryl oxidation of proteins (Haddad *et al.*, 1999).

To control the flux of ROS, aerobic cells have developed their own defence system, the antioxidant system, which includes enzymatic and non-enzymatic components. The antioxidant system consists of low molecular-wt antioxidant molecules, such as GSH and various antioxidant enzymes. SOD, the first line of defence against oxygen-derived free radicals, catalysis the dismutation of superoxide anion into H_2O_2. H_2O_2 can be transformed into H_2O and O_2 by CAT.

GSH is the most abundant nonprotein sulfhydryl containing compound and constitutes the largest component of the endogenous thiol buffer (Holmgren *et al.*, 2005). Assessment of GSH in biological samples is essential for evaluation 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). The present study recorded a significant depletion of GSH content in hepatic and lung tissues in irradiated animals as compared to control group due to oxidative stress. The depletion of GSH content in irradiated rats might be due to enhanced utilization during detoxification process or resulted from diffusion through impaired cellular membranes and or inhibition of GSH synthetase (Mohamed 2011). The resultant reduction in GSH level may thus increase susceptibility of the tissue to oxidative damage including lipid peroxidation.

A significant decrease in GSHPx activity could be attributed to the uncontrolled production of reactive oxygen species (ROS) and accumulation of H_2O_2 whereby oxidative damage to enzymes can cause a modification of their activity (Kregel and Zhang, 2007). GSH may react with H_2O_2 and lipid peroxides by action of GSHPx to reduce their toxicity (Davis *et al.*, 2001).

The significant decrease in the activity of SOD and CAT might be, also, attributed to the excess of ROS, which interacts with the enzyme molecules causing their denaturation and partial inactivation (Kregel and Zhang. 2007).

The present study found that whole-body irradiation in rats causes increases in blood sugar and decrease in insulin as Table 7. The best way to understand the dysfunction of insulin and blood sugar is the theory of oxidative stress. ROS play a role in the aetiology of several major diseases, including cancer, atherosclerosis and diabetes.

The hyperglycemia induced by gamma radiation could be attributed to the diminished utilization of glucose by irradiated tissues. Irradiation could induce the transport of certain amino acids and thus increased glucose formation through the processes of deamination and transamination (Alhersova *et al*., 1981) as well as acceleration of gluconeogenesis which resulted as an indirect effect of radiation exposure (Sedlakova *et al.,* 1998). The increase in glucose level may also be related to endocrine abnormalities induced by irradiation which promote the secretion of biologically active peptide as adrenocorticotropic hormone (ACTH) which has well documented relation to carbohydrate metabolism by promoting gluconeognesis in the liver (Harper *et al.,* 1977). Elevated glucose levels in the blood causes the sugar to chemically react with proteins of the blood vessel walls and form glycosylated proteins that subsequently causes the capillaries to swell and get easily broken (Jean-Luc and Schmidt, 2004). The radio protective activity of plant and herbs may be mediated through several mechanisms (Ganesh, 2007).

Sumac is used as a herbal remedy in traditional medicine due to its antifibrogenic, antifungal, antiinflammatory, antimalarial, antimicrobial, antimutagenic, antioxidant, antithrombin, antitumorigenic, antiviral, cytotoxic, hypoglycaemic and leukopenic (Gulmez *et al.,* 2006 and Rayne and Mazza, 2007).

Our data demonstrate that sumac extract (300 mg/ kg per animal) could act on the oxidative stress by decreasing MDA levels and nitric oxide in liver and lung tissues after gamma-irradiation. In fact, the addition of sumac extract reduced the production of NO and ROS induced by gamma rays. The action exhibited by sumac extract under our experimental conditions could be partially due to the scavenger action of its polyphenolic active constituents, phenolic acids and gallic acid (Franziska *et al.,* 2007). Gallic acid, a naturally occurring plant phenol is abundant in plants. Gallic acid is 50 times more protective than the vitamins C and E. Phenolic compounds have been considered to play an important antioxidant role as dietary antioxidants for the prevention of oxidative damage in living systems (Hertog *et al.,* 1993). The polyphenols present in the plants and herbs may up regulate the antioxidant enzymes such as CAT, GSHPx, SOD and thus may counteract the oxidative stress-induced by ionizing radiations (Ganesh, 2007). Sumac prevented depletion of GSH, GSHPx, SOD and CAT activity induced by radiation exposure (Table 3-6). The apparent protective

effect might be due to the ability of sumac to neutralize the increase in free radicals caused by radiation (AL-Jassabi and Mohd, 2010). GSH constitutes the first line of defence against free radicals in the liver and is also responsible for the maintenance of protein thiols and acts as a substrate for GSH-Px (Prakash *et al.,* 2001).

According to present study, sumac extracts causes significance increase in levels of blood sugar and decrease in insulin level in irradiated rats group as Table 7. This result agrees with Khayatnouri *et al.* (2011), who noticed that rising blood sugar more than normal range happens because of dysfunction of Insulin which regulates blood sugar. Some fruits and vegetables can stimulate insulin secretion. In this concern was found that sumac extracts of the plant have been shown to have antioxidant (Arora and Kaur, 1999), free radical scavenging (Candan, 2003) and hypoglycemic (Garrett *et al.,* 1998) biological activities. The best way to understand the dysfunction of insulin and blood sugar is the theory of oxidative stress. ROS play a role in the aetiology of several major diseases, including diabetes, cancer and atherosclerosis.

Conclusion

GSH, GSHPx, CAT and SOD protect cells against ROS. We found decreased activity of the key antioxidants, GSHPx, CAT and SOD in the liver and lung of rats treated with radiation. This indicates that the increase in MDA in the liver and lung of rats treated with radiation may be related to the decrease in the activity of SOD, CAT, GSH and GSHPx which scavenge hydroperoxides and lipid peroxides. Our data indicate that sumac could maintain the endogenous antioxidant defence mechanism in rats and protect the animals from radiation-induced liver and lung toxicity. Moreover, sumac may protect against ionizing radiation-induced lung damage because of its antioxidant effect.

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أزهار السماق المجففة تحمى الجرذان البيضاء من الأثار الناتجة للاشعاع

منال محمد درويش

قسم بيولوجيا الإشعاع ، المركز القومي لبحوث وتكنولوجيا الإشعاع ، ص. ب. ٢٩ مدينة نصر ، ناقاهرة ، مصر.

الهدف من هذا البحث توضيح تأثير السماق كمضاد للأكسدة في تنظيم الضرر التأكسدي في أنسجة الكبد والرئة للجرذان المعرضة لجرعة واحدة (٥ جراي) لأشعة جاما.

وقد قسمت ٤٨ من الجرذان بالتساوى إلي ٤ مجاميع: المجموعة الأولي وهي الضابطة والمجموعة الثانية المعالجة بالسماق ، فتم إعطاؤها ٣٠٠ مليجرام لكل كيلو جرام من وزن الجسم يومياً ولمدة عشرة أيام متتابعة. والمجموعة الثالثة عرضت لجرعة مقدارها ٥ جراي من أشعة جاما وأخيرا المجموعة الرابعة التي تم إعطاؤها ٣٠٠ مليجرام لكل كيلو جرام من وزن الجسم يومياً ولمدة عشرة أيام متتابعة وعرضت لجرعة ٥ جراي من أشعة جاما بعد جرعة يومية من السماق لمدة ٣ ايام. تم ذبح الجرذان فى اليوم الأول والسابع على التوالى من تعرضها للإشعاع. وقد جمعت عينات و أظهرت النتائج زيادة معنوية في محتوى (الملوندای الدهايد و النيترك أوكسيد) في أنسجة الكبد والرئة نتيجة لتعرضها لأشعة جاما. وانخفاض معنوي في محتوى (الكاتليز و الثيوباربتيورك اسيد ، الجلوتاثيون بيروكسيديز و الجلوتاثيون) في أنسجة الكبد والرئة. كما اظهرت النتائج زيادة في الجلوكوز يصاحبها نقص فى مستوى الأنسولين.

وقد أظهرت الدراسة ان اضافة السماق لمدة ١٠أ يام مع التعرض لأشعة جاما ادى الى تحسن ملحوظ ماعدا مستوى الجلوكوز .

من هذه الدراسة يمكن التوصية باستخدام السماق كمضاد للأكسدة لحماية الأعضاء الهامة في الجسم ووظائفها من تأثير أشعة جاما كذلك قام السماق بزيادة مستوي الجلوكوز في الدم لذلك ينصح مرضى السكر بأخذ ذلك فى الأعتبار.