

Evaluation of the possible Immunomodulatory and Neuroprotective effects of γ -irradiated basil (*Ocimum basilicum*) against arsenic toxicity in rats

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Research

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Abstract

In view of the widespread incidence of arsenic poisoning around the world, it was necessary to study this phenomenon and analyze it to find out how to treat it through the application of alternative medicine, which has spread its use significantly in the world using herbs and plants. Gamma irradiation as a phytosanitary treatment of food and herbal materials is increasingly recognized throughout the world by improving their hygienic quality. The aims of this study to evaluate the therapeutic effect of raw or irradiated basil on rats exposed to arsenic toxicity. Basil was irradiated by gamma rays at dose 10 KGy. Forty-eight adult Wistar albino rats were divided into six groups as follows group-1: Control group, group-2: received 400 mg/ kg of aqueous extract of basil, group-3: received 400 mg/ kg of aqueous extract of irradiated basil, group- 4: received 10 mg/kg of sodium arsenate solution, group- 5: received 10 mg/kg of sodium arsenate solution and 400 mg/ kg of aqueous extract of basil, and group- 6: received 10 mg/kg of sodium arsenate solution and 400 mg/ kg of aqueous extract of irradiated basil. At the end of the experiment (5 weeks), the rats were sacrificed, blood and brain tissue samples were subjected to estimate of the following: CBC, inflammatory markers (CRP, TNF- α , and IL6), immunoglobulin markers (IgA, IgG, IgM), and the levels of oxidative stress and antioxidant in brain tissue (MDA, CAT, SOD, and GSH). The results showed a rise in the antioxidant of basil after the irradiation process. The arsenic caused a significant decreased in levels of HB, RBC, LYM, NEU and PLT, while the increased levels of WBC and reticulocyte count as compared to the control group. Also, the rats exposed to arsenic showed a significant increase in inflammatory markers, immunoglobulin markers in serum, and oxidative stress accompanied with significant decreased in antioxidant in the brain. In contrast, the administration of basil extract along with arsenic was a helpful factor in alleviation of these side effects. In conclusion, our findings showed that the irradiation process enhanced antioxidants in basil plants. Furthermore, basil has ability to attenuated arsenic toxicity.

Introduction

Arsenic is a toxic substance that occurs naturally and is found in water, rock soil and many foods (Duker et al., 2018). Arsenic toxicity affects millions of people in different parts of the world through the ingestion of arsenic-contaminated drinking water and food (Huq et al., 2006; Flanagan, Johnston and Zheng, 2012). In recent years, arsenic toxicity has created significant public concern (Duker et al., 2018). It has no taste or smell, which makes it particularly hazardous, so you can be exposed to it without knowing it (ATSDR, 2017). So, the increasing presence of an amount of arsenic in the environment present major risks, as exposure through inhalation, ingestion and dermal contact can cause various adverse effects on health (Vimercati et al., 2017). From these adverse health effects, the disorders of the nervous system (Mochizuki et al., 2019), immune system (Tutkun et al., 2019), digestive system (Chiocchetti, Vélez and Devesa, 2018), and respiratory system (Zhao et al., 2019). To treat these disorders has suggesting used complementary and alternative medicine (CAM) that may be as helpful.

The National Center for CAM (NCCAM) describes (complementary and alternative medicine) as a category of healthcare and medical systems (NCCIH, 2018). A systemic review conducted by Eardley et

al. (2012) found that, for many reasons, people are using CAM, including its availability, perceived health, and disease prevention. As one of the main forms of CAM is herbal medicines, which uses parts of a plant or whole plants to avoid and cure diseases (Bent, 2008; Pan et al., 2014). The herbal medicinal products are characterized by the presence of complex chemical compounds responsible for the pharmacological activities that contribute to health benefits (Bent, 2008). Basil plants considered from herbal medicine that has eminence value as a cure for various diseases (Patel et al., 2018).

Basil (*Ocimum basilicum* L.) is an herbaceous and aromatic plant worldwide cultivated which belongs to the *Lamiaceae* family (Jakovljević et al., 2016). It has several therapeutic properties including antioxidant, anti-aging, anticancer, antiviral, antimicrobial, anti-genotoxic, and anti-inflammatory (Sakr and Al-Amoudi, 2012; Shirazi et al., 2014). Studies have shown many pharmacological effects for basil in several diseases such as liver fibrosis (Alomar and Al-Attar, 2019), diabetes mellitus (Widjaja and Rusdiana, 2019), asthma (Eftekhar et al., 2019), anemia (Zangeneh et al., 2019), and cerebral injury (Singh, Krishan and Shri, 2018). Based on the pharmacological and therapeutic properties, basil has played an important role in both traditional pharmaceutical products and contemporary pharmacological and clinical science (Shirazi et al., 2014). But there may be concerns about the use of herbs, which is that herbs are susceptible often to contamination during processing or storage by micro-organisms and insect pests. This leads to shortens their shelf life and triggering serious illness in some cases, particularly if the herbs contaminated with *Salmonella* and *Staphylococcus aureus* (Chatterjee et al., 2016). Thus, herbs should be subjected to sterilization or microbial treatment before use.

There are various techniques for the decontamination of medicinal plants, including irradiation (Garg and Gupta, 2016). This is a physical process that applies high-energy ionizing radiation to the plants in order to enhance their safety and shelf-life (Byun et al., 1999; SádEcká, 2007; Alothman, Bhat and Karim, 2009). In particular, gamma irradiation seemed to be the best way to decontaminate herbs from microbes without triggering quality changes (Lee, Lee and Kim, 2005). As the absorbed energy of radiation can break the bonds of DNA molecules in microorganisms present in the product and inactivates certain enzymes, this greatly reduced its damaging impact on products. Not only microorganisms are destroyed, but even gametes, insects and parasites are prevented from reproducing, resulting in various preservative effects (Farkas, 2006). Moreover, irradiation serves as a safe technique in food processing supported by many internationally recognized organizations, where joint (Food and Agriculture Organization/ International Atomic Energy Agency/World Health Organization) Expert Committee on the Wholesomeness of Irradiation of Food has ruled that food subject to low irradiation dosage (up to 10 kGy) is safe and not need any testing of toxicology (Wen et al., 2006).

The present study was therefore designed to evaluate the possible immunomodulatory and anti-inflammatory effects of raw and irradiated basil (*Ocimum basilicum*) against arsenic toxicity in rats.

Materials And Methods

2.1 Materials

2.1.1 Chemicals and kits

Sodium arsenate was obtained from British Drug Houses (BDH) chemical company, England, UK. Diethyl ether was obtained from Sigma-Aldrich company, Louis, USA. Kits for assays of immunoglobulin G (IgG), immunoglobulin M (IgM), immunoglobulin A (IgA), tumor necrosis factor-alpha (TNF α), interleukin (IL-6), C-reactive protein (CRP), superoxide dismutase (SOD), glutathione (GSH), catalase (CAT) and malondialdehyde (MDA) were obtained from Abcam Chemical Company, Cambridge, UK. Kits for assay Total capacity antioxidant were obtained from Cell Biolabs company, California, USA. Kits assay protein concentration in tissues (Pierce™ BCA Protein Kit) was obtained from Thermo Fisher Scientific company, Waltham, US.

2.1.2 Plant material

The basil (*Ocimum basilicum*) leaves were purchased from the local traditional market in Jeddah, Saudi Arabia.

2.1.2.1 Gamma Irradiation treatment

The samples of dry basil powder were irradiated with 10 KGy of gamma rays after the leaves were transferred into polyethylene bags, using a Cobalt-60 source at a dose rate of 4.75 KGy/h at the National Centre for Radiation Research and Technology (NCRRT), Nasr City, Cairo, Egypt.

2.1.3 Experimental animals

The study will be carried out using adult female Wistar rats weighing (150–200 g); they were obtained from faculty of pharmacy at King Abdulaziz University. The animals were housed in cages and received normal rat chow and tap water in a constant environment (room temperature 28 ± 2 °C, room humidity $60 \pm 5\%$) in a 12 h light and 12 h dark cycle. Rats were kept under supervision for two weeks before the experiments started and during all stages of the whole experiment. Animal's procedures were performed in accordance with the Ethics Committee of the King Fahad Medical Research Center and in accordance with the recommendations for the proper care and use of laboratory animals.

2.2 Methods

2.2.1 Preparation of basil extracts

The water extracts of raw or irradiated dried basil leaves were prepared according to the method described by Ghazwani, Osman and Balamash (2020).

The total antioxidant capacity was measured in basil extracts using the Total Capacity Assay kit with CAT# STA-360.

2.2.2 Experimental Design

In the experiment, 48 rats were divided into six groups each of 8 rats as follows:

Group 1: normal control rats were given only distilled water.

Group 2: rats received 400 mg/ kg of aqueous extract of raw basil (Ezeani et al., 2017) .

Group 3: rats received 400 mg/ kg of aqueous extract of irradiated basil (Ezeani et al., 2017).

Group 4: rats received 10 mg/kg of sodium arsenate solution (Firdaus et al., 2018).

Group 5: rats received 10 mg/kg of sodium arsenate solution and 400 mg/ kg of aqueous extract of basil.

Group 6: rats received 10 mg/kg of sodium arsenate solution and 400 mg/ kg of aqueous extract of irradiated basil.

All doses were given through an oral gastric tube daily for five weeks.

At the end of the experiment, rats fasted overnight for scarification. Blood samples were withdrawn by a heparinized capillary tube from the retro-orbital plexus of each rat under anesthesia with diethyl ether, it is put into two tubes, one is ethylenediamine tetra-acetic acid (EDTA) tube and the other is a serum-separating tube. The EDTA tube immediately turned to lab analysis while serum-separating tube centrifuged at 3000 rpm for 15 min to separate serum and then stored at -40° C until the biochemical analysis is done. Directly after preparing the blood sample, rats sacrificed and the brain was kept in ice for homogenate preparation.

2.5. Biochemical analysis

The biochemical analysis for complete blood count (CBC) were done in Kingdoms Labs. The blood serum IgG, IgM and IgA, TNF α , IL-6 and CRP were identified using the kits with CAT# ab189578, ab157735, ab157738, ab46070, ab119548, and ab108827, respectively. For tissue analysis, the brain was homogenized and estimated each of SOD, GSH, CAT and MDA according to the kits with CAT# ab65354, ab138881, ab83464, and ab118970, respectively, while the protein concentration estimated in the brain was used Kits with CAT# 23225.

2.6. Statistical analysis

The data of each group were analyzed using MegaStat 9.4 (add-in for Excel). The data were expressed as arithmetic mean and standard deviation of the mean (SD). Differences between groups were analyzed for parametric parameters using one-way variance analysis (ANOVA), the least significant difference equation (LSD). A *P* value below or equal to 0.05 was considered significant.

Results

3.1. Antioxidant in irradiated plant leaves

The effect of irradiation on antioxidants is showed in Fig. 1. Where leaves treated with gamma irradiation (10 kGy) showed a change, a 10.3% increase in the content of total antioxidants compared to raw leaves not treated with radiation.

3.2. Complete blood count (CBC)

The effects of aqueous extracts of raw basil or irradiated basil for 5 weeks on the levels of hemoglobin (HB), red blood cells (RBC), hematocrit (HCT), platelets (PLT), White blood cells (WBC), WBC differential and reticulocyte count in rats exposed to arsenic are present in Tables 1 and 2.

No effect of raw or irradiated basil administration in normal animals on all previous parameters was noted. Rats, which were exposed to arsenic showed a significant decrease in levels of HB, RBC, PLT, neutrophils (NEU), and lymphocytes (LYM) compared to the control group. While there was a marked increase in the levels of HCT, WBC, monocytes (MON) and reticulocyte count compared to the control group. Administration of raw and irradiated basil along with arsenic significantly reduced arsenic toxicity effect by the improvement levels of these parameters.

Table 1
Effect of basil extracts on hematological parameters of rats exposed to arsenic

	HB (g/dl)	RBC (10 ⁶ / mL)	HCT (%)	PLT (10 ³ / mL)
C	12.661 ± 1.258	4.450 ± 0.575	29.635 ± 1.870	263.13 ± 52.58
B	12.725 ± 0.902 bbb	4.570 ± 0.491 bbb	29.286 ± 0.516 bbb	274.50 ± 19.17 bbb
IB	12.810 ± 0.756 bbb	4.568 ± 0.487 bbb	29.518 ± 0.908 bbb	277.25 ± 13.63 bbb
A	8.748 ± 0.590 aaa	3.100 ± 0.524 aaa	39.058 ± 0.655 aaa	143.25 ± 7.96 aaa
B + A	10.918 ± 0.713 aaa bbb	4.066 ± 0.463 bbb	30.978 ± 1.748 bbb	188.38 ± 10.89 aaa bb
IB + A	11.249 ± 0.290 aa bbb	4.151 ± 0.164 bbb	32.330 ± 1.863 aaa bbb	177.88 ± 10.47 aaa bb

Values are the mean of 8 observation ± SD.

Significant different from C value at $P < 0.05^a$, 0.01^{aa} , 0.001^{aaa}

Significant different from A at value at $P < 0.05^b$, 0.01^{bb} , 0.001^{bbb}

Table 2
Effect of basil extracts on hematological parameters of rats exposed to arsenic

	WBC (10^3 / mL)	WBC differential			Reticulocyte Count (%)
		NEU (%)	LYM (%)	MON (%)	
C	5.661 ± 0.508	62.403 ± 1.869	28.16 ± 2.658	4.113 ± 0.631	1.413 ± 0.416
B	5.255 ± 0.532 bbb	63.388 ± 1.886 bbb	27.61 ± 4.022 bb	4.250 ± 0.460 bbb	1.100 ± 0.185 bbb
IB	5.134 ± 0.604 bbb	64.538 ± 1.577 bbb	29.46 ± 4.530 bbb	4.064 ± 0.261 bbb	1.263 ± 0.424 bbb
A	9.761 ± 0.893 aaa	38.051 ± 2.361 aaa	20.00 ± 2.624 aaa	7.150 ± 0.493 aaa	2.350 ± 0.540 aaa
B+A	6.160 ± 0.825 bbb	54.175 ± 5.389 aaa bbb	24.95 ± 5.687 b	5.163 ± 0.460 aaa bbb	1.011 ± 0.110 bbb
IB+A	5.978 ± 0.610 bbb	51.850 ± 5.011 aaa bbb	25.73 ± 5.035 b	5.113 ± 0.500 aaa bbb	1.163 ± 0.518 bbb

Values are the mean of 8 observation ± SD.

Significant different from C value at $P < 0.05^a$, 0.01^{aa} , 0.001^{aaa}

Significant different from A at value at $P < 0.05^b$, 0.01^{bb} , 0.001^{bbb}

3.3 Antibodies

The extract of each raw and irradiated basil had distinct effects on antibodies in rats exposed to arsenic that are showed in Table 3.

The treatment with raw or irradiated basil to normal animals not producing an effect on levels of serum IgG, IgM and IgA. The arsenic group showed a significant decrease in IgG, IgM and IgA levels compared to the control group. The treatment with basil extract as raw or irradiated along with arsenic dose was

showed a significant increase in those antibodies' levels, compared with the group of rats given only arsenic.

Table 3
Effect of basil extracts on immunoglobulins of rats exposed to arsenic

	IgG ($\mu\text{g/ml}$)	IgM ($\mu\text{g/ml}$)	IgA ($\mu\text{g/ml}$)
C	517.16 \pm 35.137	0.628 \pm 0.084	90.180 \pm 6.688
B	522.490 \pm 41.527 bbb	0.640 \pm 0.053 bbb	93.236 \pm 7.697 bbb
IB	514.663 \pm 32.665 bbb	0.655 \pm 0.064 bbb	94.614 \pm 5.087 bbb
A	202.500 \pm 40.818 aaa	0.226 \pm 0.024 aaa	45.779 \pm 5.816 aaa
B + A	298.911 \pm 32.731 aaa bbb	0.389 \pm 0.015 aaa bbb	72.754 \pm 4.942 aaa bbb
IB + A	287.915 \pm 35.128 aaa bbb	0.408 \pm 0.021 aaa bbb	76.745 \pm 4.229 aaa bbb
<i>Values are the mean of 8 observation \pm SD.</i>			

Significant different from C value at $P < 0.05^a$, 0.01^{aa} , 0.001^{aaa}

Significant different from A at value at $P < 0.05^b$, 0.01^{bb} , 0.001^{bbb}

3.4 Inflammatory markers

The level of markers of inflammation in rats exposed to arsenic which received raw or irradiated basil as a treatment showed in Table 4.

In normal animals, the administration of raw or irradiated basil has not had an effect on the levels of serum TNF, IL-6 and CPR. The rats exposed to arsenic showed a significant increase in levels of TNF, IL-6, and CPR as compared to the control group. While giving raw or irradiated basil extract was noted significantly reduced in these inflammatory markers induced by arsenic.

Table 4
Effect of basil extracts on the inflammation markers of rats exposed to arsenic

	TNFα (pg/ml)	IL-6 (pg/ml)	CRP (ng/ml)
C	17.829 \pm 1.221	21.048 \pm 2.134	0.134 \pm 0.039
B	16.144 \pm 1.428 bbb	20.753 \pm 1.962 bbb	0.134 \pm 0.034 bbb
IB	16.123 \pm 1.216 bbb	20.456 \pm 2.940 bbb	0.140 \pm 0.018 bbb
A	40.043 \pm 2.453 aaa	35.334 \pm 3.973 aaa	0.990 \pm 0.076 aaa
B + A	27.656 \pm 2.173 aaa bbb	27.413 \pm 3.842 aaa bbb	0.660 \pm 0.093 aaa bbb
IB + A	28.935 \pm 2.634 aaa bbb	26.876 \pm 1.563 aaa bbb	0.490 \pm 0.033 aaa bbb
<i>Values are the mean of 8 observation \pm SD.</i>			

Significant different from C value at $P < 0.05^a$, 0.01^{aa} , 0.001^{aaa}

Significant different from A at value at $P < 0.05^b$, 0.01^{bb} , 0.001^{bbb}

3.4 Antioxidants and oxidative damage

The results of determining the content of SOD, GSH, CAT and MDA in rats given arsenic along with raw basil or irradiated basil were shown in Table 5.

The normal rats treated with irradiated basil showed an increase in the level of SOD than rats treated with raw basil. The level of GSH was showed an increase in normal rats of both of raw basil group and irradiated basil group as compared to the control group. Arsenic-exposed rats showed a significant increase in MDA levels accompanied by a significant decrease in SOD, GSH and CAT compared to a control group. The management of raw or irradiated basil along with arsenic alleviated the effects of arsenic and resulted in a significantly decreased MDA with significantly increased SOD, GSH, CAT.

Table 5

Effect of basil extracts on the antioxidants and oxidative damage in the brain of rats exposed to arsenic

	SOD (Inhibition rate % / mg of protein)	GSH ($\mu\text{M}/\text{gram}$ tissue)	CAT ($\mu\text{M}/\text{mg}$ of protein)	MDA ($\mu\text{M}/\text{mg}$ of protein)
C	105.406 \pm 7.342	90.743 \pm 7.044	0.020 \pm 0.003	2.496 \pm 0.451
B	107.548 \pm 9.384 bbb	96.709 \pm 3.420 a bbb	0.019 \pm 0.004 bbb	2.400 \pm 0.422 bbb
IB	114.655 \pm 8.165 a bbb	95.425 \pm 4.426 a bbb	0.021 \pm 0.004 bbb	2.441 \pm 0.433 bbb
A	77.977 \pm 10.370 aaa	60.248 \pm 2.657 aaa	0.009 \pm 0.000 aaa	6.005 \pm 0.126 aaa
B + A	82.049 \pm 8.953 aaa bbb	84.259 \pm 4.487 aa bbb	0.012 \pm 0.001 aaa	3.479 \pm 0.610 aaa bbb
IB + A	89.249 \pm 9.381 aaa bbb	82.533 \pm 3.153 aa bbb	0.014 \pm 0.003 aa bb	3.165 \pm 0.484 aa bbb
<i>Values are the mean of 8 observation \pm SD.</i>				

Significant different from C value at $P < 0.05^a$, 0.01^{aa} , 0.001^{aaa}

Significant different from A at value at $P < 0.05^b$, 0.01^{bb} , 0.001^{bbb}

Discussion

4.1. Antioxidant in irradiated plant leaves

The irradiation treatment can increase the content of some phytochemicals and the plant's antioxidant activity, thereby increased biological value (Zevallos-Concha et al., 2016; Pereira et al., 2018). The results indicated that the extract of irradiated basil showed a highly significant increase in total antioxidants as a comparison to raw basil. Similar observations were reported in previous studies on basil and some other plants (Khawory et al., 2020; Osman, Ghazwani and Balamash, 2020; Rady et al., 2020).

Basil contains phenolic compounds and flavonoids (Bahcesular et al., 2020), that are considered as natural antioxidants. These biomolecules exhibit their activity through various mechanisms, including inhibiting enzymes that inducing free radical produce, increasing endogenous antioxidants, removing free radicals, and inducing the expression of the numerous genes responsible for enzyme synthesis that inhibit oxidative stress (Primiano, Sutter and Kensler, 1997). Ghazwani, Osman and Balamash (2020) reported that the Fourier-transform infrared (FTIR) analysis indicated to increase the content of phenolic acids and flavonoids in basil leaves after treated with 10 kGy of gamma-ray. Moreover, Maraiei, Khaled and Elsayy (2017) reported that the gamma irradiation-induced the biosynthesis of certain phenolic compounds. Also, it seems that gamma irradiation with 10 kGy might stimulate some chemical reactions in basil, which perhaps increase in phenolic content by the breakdown of covalence bonds among phenolic components and, free phenolic components with low molecular weight are increasing (Jamshidi, Barzegar and Sahari, 2014).

4.2. Complete blood count (CBC)

A complete blood count test is a blood test used to assess general health and detect a range of disorders in hematological parameters. A complete blood count test measures many blood components and features, including red blood cells that carry oxygen, white blood cells that fight infection, hemoglobin that oxygen-carrying protein in red blood cells, hematocrit that indicate to the ratio of red blood cells to the liquid or plasma component of the blood and platelets that help blood clot, and that any change whether an abnormal rise or decrease in the census, indicate the incidence of diseases or disorders requiring medical procedures (Clinic, 2018).

In our study, it has been observed that the levels of HB, RBC, PLT, NEU, and LYM are decreased significantly with a marked increase in the HCT, WBC, MON and reticulocyte count in rats exposed to arsenic compared to the control group. The results are consistent with some studies (Kajiguchi et al., 2005; Bhattacharya and Halder, 2012; Sumedha and Miltonprabu, 2013; Lemaire et al., 2015; Ghosh et al., 2017; Su et al., 2018). This effect of Arsenic exposure on the hematopoietic system may be attributed to the mechanisms of arsenic toxicity which may induce hemolysis and erythrophagocytosis through increased oxidation of sulfhydryl groups in hemoglobin and decreased oxygen intake by cells as a result of decreased intracellular glutathione, which decreases the lifespan of erythrocytes (Abdul et al., 2015). Moreover, arsenic exposure can also cause a range of changes, such as increasing ceramide formation, membrane disintegration, cytosolic calcium levels, besides decreasing in adenosine triphosphate (ATP) levels, cell membrane integrity affecting erythrocyte lifespan (Abdul et al., 2015).

Regarded the change in platelet count, this confirmed that arsenic inhibited platelet differentiation within the hematopoietic system of bone marrow, leading to reduced platelet production (Wu et al., 2014).

The white blood cell level was decreased in arsenic feed groups. It might be due to the impact of arsenic which induced apoptotic effect on plasma cells as noted by Rousselot et al. (2004). WBC may generally be divided into five classes, based on their function, morphology and origin: LYM, MON and NEU (Villa et

al., 2003). The changes in the LYM and NEU populations present in this study may be due to arsenic caused immune inhibition in rats (Taheri et al., 2016).

Our findings demonstrated that extracts of basil caused improved the disorders that occur in CBC. This is in agreement with the results of previous researches (Ofem, Ani and Eno, 2012; Zangeneh et al., 2019). This effect may due to basil which contains a proportion of iron (Nworgu, Yekini and Oduola, 2013), that contributes to improving the level of HB in the blood and has the ability to stimulate production and increase of RBC to treat deficiency caused by arsenic. Furthermore, in normal, the lack of oxygen in the local tissue appears to lead to the production of glycoprotein known as erythropoietin, which induces increased erythrocyte output (Bowman and Rand, 1980). Basil leaves extract is very likely to contain erythropoietin-like agents that are responsible for increased erythrocyte production (Ofem, Ani and Eno, 2012). Saha et al. (2012) reported that secondary metabolites of basil, consisting of important elements include essential oil geraniol, a monoterpene and citral, play a role as the modulator in hematological abnormalities (Ofem, Ani and Eno, 2012). Moreover, in results about the increased lymphocyte count after basil administration, it has been reported that *Ocimum basilicum* modulates the cell-mediated as well as a humoral immune response that could be due to the presence of flavonoids and terpenoids (Mediratta, Sharma and Singh, 2002).

4.3 Antibodies

Antibodies also are known as immunoglobulins, are substances made by the body's immune system in response to foreign substances. Antibodies bind to these foreign substances and they can be killed by the immune system. IgG, IgM and IgA from the major types of antibodies. If reduced levels of antibodies produced by the immune system, it leads to more likely to develop repeated infections (Staff, 2019).

The results of our study showed that in the arsenic group of rats (10 mg/kg BW) a highly significant reduction was observed in IgG, IgA and IgM levels compared to the control group. The results are consistent with some studies (Institoris et al., 2001; Sankar et al., 2013). The effect on immunoglobulin levels associated with arsenic exposure can attribute to the arsenic disrupts glucocorticoid regulation, responsible for immune function (Kaltreider et al., 2001). Furthermore, the apoptosis caused by arsenic may result in decreased immune responses (Harrison and McCoy, 2001).

The administration of water extract from raw or irradiated basil extract demonstrated a protective effect against arsenic toxicity in rats, by increasing antibodies that decreased as a result of arsenic poisoning. These results are in line with the findings of Mohammed, Kadhim and Taher (2017) and Jahejo et al. (2019). Jeba, Vaidyanathan and Rameshkumar (2011) showed that aqueous extract of basil stimulated the antibody production in rats. The flavonoids present in the basil leaves are mainly responsible for the immunomodulatory effect (Ravindran, 2017).

4.4 Inflammatory markers

Inflammation is a biological response of the immune system which can be induced by damaged cells, toxic compounds or pathogens (Medzhitov, 2010). It is part of the body's defense mechanism. one of the

major aims of inflammation is to bring immune cells to the area of concern as well as to inactivate or destroy any injurious stimuli and to also begin the repair (Ferrero-Miliani et al., 2007; Medzhitov, 2010). The inflammation response is caused by specific immune factors released from the damaged cells. Where, the damaged cells release cytokines, including interleukins, such as IL-6, IL-8, and tumor necrosis factor- α , that are responsible for communication between white blood cells. Interleukins also stimulate the production and release of CRP from the liver; an important component of the innate immune system (Sinclair, Wang and Tetrack, 2012).

Usually, molecular and cellular activities and interactions efficiently alleviate inevitable infection or damage, during acute inflammatory responses. This effect helps restore homeostasis in the tissue and overcome the acute inflammation. Uncontrolled acute inflammation can become chronic, however, and can lead to a number of chronic inflammatory diseases (Zhou, Hong and Huang, 2016). The elevated levels of inflammatory markers are expected to be associated with toxic metals exposure.

Results of this study showed that serum IL-6, TNF- α and CRP level in rats exposed to arsenic was highly significantly elevated. Our findings agree with the results of the previous study on the association between arsenic and ability to cause chronic inflammation by demonstrating the increased pro-inflammatory mediators like TNF- α , IL-6 and CRP in the arsenic exposed group in comparison to the control group (Prasad and Sinha, 2017). Inflammation considered to be one of the main arsenic toxicity mechanisms that can be correlated with increasing cellular damages, oxidative stress and lipid peroxidation (Bhadauria and Flora, 2007).

In this work also, it was demonstrated that oral treatment with basil extracts diminished inflammations in rats exposed to arsenic. These results in agreement with Aye et al. (2019) and Takeuchi et al. (2020) who found that basil has anti-inflammatory effects. Rodrigues et al. (2016) reported that the basil essential oil was effective in reducing inflammations (acute or chronic) by induced inhibiting of the inflammatory mediator receptors and the migration of cells to stimulus locations. This may be attributed to the contains of basil of rosmarinic acid (Kwon et al., 2019), where this compound has been related to anti-inflammatory activities (Luo et al., 2020).

4.5 Antioxidants and oxidative damage

Antioxidants are considered the enzymes of the body's protection, are able to stabilize free radicals before attacking components of the cell. They work to diminishing free radicals through reducing their energy or donate electrons to them, thus making it stable (Krishnamurthy and Wadhvani, 2012). While, "oxidative stress, defined as a disturbance in the balance between the production of reactive oxygen species (free radicals) and antioxidant defenses" (Betteridge, 2000).

In the present study, observed a very highly significant decrease in GSH, SOD and CAT accompanied by increased MDA of the rat's brain in the arsenic group as compared to the normal control group. This result is similar to the study of Sun et al. (2018) that reported that arsenic caused significantly decreased GSH, SOD and CAT with increased MDA content in the brain tissues of chickens. This may be attributed to the

toxic effect of arsenic that may induce oxidative stress by interacting with antioxidants, resulting in the accumulation of free radicals in cells (Bonetto, Villaamil Lepori and Puntarulo, 2014).

In contrast, basil giving a positive effect on the brain by improving the levels of antioxidant antioxidants, and fat oxidation (MDA). These results were in line with recent studies showed that the water extract of gamma-irradiated basil contributes to improving the oxidative stress induced by arsenic exposure in rats (Ghazwani, Osman and Balamash, 2020; Osman, Ghazwani and Balamash, 2020). Also agree with the results of Khodabakhshi et al. (2017), who proved that the increased level of MDA in the mice brain tissue following seizures was prevented by basil extract. Moreover, Khaki (2016) demonstrated that the basil extract protects brain cells from the harmful effects by regulating the antioxidant enzymes in the serum. This saves the neurons from irreversible cell injury. The antioxidant effect is due primarily to phenolic elements, such as, phenolic acids and flavonoids, which have redox properties and ability to neutralize free radicals (Shahidi, Janitha and Wanasundara, 1992).

Conclusion

In this study, we demonstrated that gamma radiations have the ability to increases antioxidants contents in basil leaves. Moreover, the water extracts obtained from *Ocimum basilicum* can be successful in diminished arsenic toxic effect through the improvement of the homeostasis of CBC and immunoglobins level, reduced inflammatory markers and, enhancement ability of antioxidants to be overcome oxidative stress in the brain.

Declarations

Ethical approval and consent to participate:

This article prepared by Mrs. Batoul Sami Amjad with the participation of a number of authors who contributed to the audit, review and supervision.

Consent for publication:

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The full research facility contains all the data and materials used in the study

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Abbreviations

AAP	4-aminophenzone
ADP- ribose	Adenosine diphosphate ribose
ALP	Alkaline phosphatase
ALT	Alanine Aminotransferase
AM	Alternative Medicine
AOM	Azoxymethane
AS	Arsenic
AST	Aspartate Aminotransferase
B Cells	B lymphocytes (a type of white blood cell of the lymphocyte subtype)
Basil	Ocimum basilicum
BCP	Beta-caryophyllene
BHT	Butylated hydroxytoluene
CAT	Catalase
CCl ₄	carbon tetrachloride
CRP	C-Reactive Protein
C _s	Cesium-137
DHBS	Dichloro -2-hydroxybenzene sulfonic acid
⁶⁰ Co	Cobalt-60
DM	Diabetes Mellitus
DNA	Deoxyribonucleic acid
ELISA	Enzyme-Linked Immunosorbent Assay
EMG	Electromyography
g	gram
GC	Gas Chromatography
GC/MS	Gas Chromatography/Mass Spectrometry
GPx	Glutathione Peroxidase
GRD	Glutathione Reductase
GSH	Reduced Glutathione
GSR	Glutathione Reductase

GSSG	Glutathione disulfide
GST	Glutathione S-Transferase
H ₂ O	Water
H ₂ O ₂	Hydrogen Peroxide
HAase	Hyaluronidase
HB	Hemoglobin
HBPP	Human Brain Proteome Project
HCT	Haematocrit
HRP	Enzyme Horseradish Peroxidase
IgA	Immunoglobulin G (Immunoglobulin A is an antibody)
IgG	Immunoglobulin G, is a type of antibody
IgM	immunoglobulin M Antibody
IL-1	The Interleukin-1
IL-6	Interleukin-6
KCl	Potassium chloride
Kg	Kilograms
L	liter
LOP	Lipid peroxidation
LPO	Lipid Peroxidation
LSD	Least Significant Difference
MAPKs	Mitogen Activated Protein Kinases
MDA	Malondialdehyde
mM	Macromolecule
mmol/L	Millimoles per Liter
mRNA	Messenger Ribonucleic acid
MS	Mass spectrometry
Na ₃ AsO ₄	Sodium Arsenate solution
NADPH	Nicotinamide Adenine Dinucleotide Phosphate
NaHCO ₃	Sodium bicarbonate

NBT	Nitroblue tetrazolium
NCRRT	National Centre for Radiation Research and Technology
nm	nanometer
nmol/mg	nanomole per milligram
NO	Nitric Oxide
NO.	Number
NOS	Nitric Oxide Synthase
O [•]	Oxygen Free Radical
O ₂	Oxygen
O ₂ ⁻	Superoxide
OBO	Ocimum basilicum oil
OC	Oral Contraceptive
°C	Celsius
OGTT	Oral Glucose Tolerance Test
OH [•]	Hydroxyl
OS	Oxidative Stress
PARP	Polymerase
PBS	Phosphate Buffered Saline
pg/ml	Picogram per milliliter
pH	a scale of acidity from 0 to 14
PLT	Platelets
PMS	Phenazine methosulphate
PMSF	Phenylmethylsulfonyl fluoride
RBC	Red Blood Cells
RCOOH	Carboxylic Acid
RNA	Ribonucleic acid
RNS	Reactive Nitrogen Species
ROS	receptive oxygen species

ROS	Reactive Oxygen Species
SD	Sexual dysfunction
SOD	Superoxide Dismutase
STZ	Streptozotocin
STZ	Streptozotocin
T Cells	T lymphocyte, is a type of lymphocyte (a subtype of white blood cell)
TAC	total antioxidant capacity
TBARS	Thiobarbituric Acid Reactive Substances
TCA	Trichloroacetic
TNF α	Tumor necrosis factor alpha
Tris/HCl	Tris Hydrochloride
Triton X-100	A Commonly Used Detergent In Laboratories
USEPA	U.S. Environmental Protection Agency
WBC	White Blood Cell
WHO	World Health Organization
β	Beta
β -ME	β -Methylphenethylamine
μ /dl	Milligram per deciliter
μ g	Microgram
μ L	microliter

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Figures

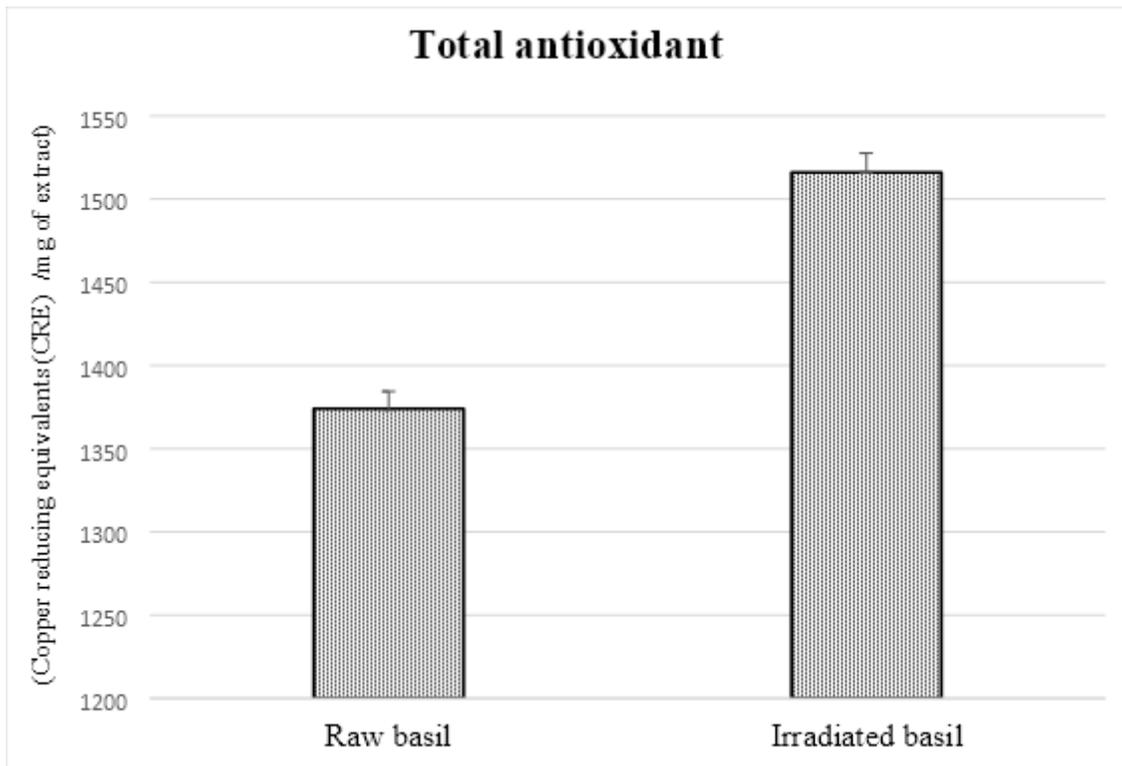


Figure 1

Total antioxidants in raw and irradiated basil

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