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Radioprotective Potencies of Allium Cepa Extract (ACE) against Radiation-Induced Hepatoxicity in Wistar Rats

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Abstract

Background and Purpose: All types of ionizing radiations generate ions which can lead to the formation of free radicals and reactive oxygen species (ROS). Excess production of free radicals or decrease in antioxidants level leads to oxidative stress. It is a harmful process that induces damage to cell structures, lipids, proteins, RNA and DNA which leads to a number of diseases. The aim of this study is to examine the effect of plant extract (Allium Cepa Extract (ACE)) on the kidney of wistar rats exposed to radiation using and assaying some biochemical enzymes. **Material and Method:** 60 wistar rats weighing 170 ± 20 g were equally divided into six groups for the study. Group 1 (control): neither received ACE nor irradiation. Group 2 (ACE): received 1000 mg/Kg b.wt of ACE. Group 3 (4 Gy-Irradiated): were exposed to 4 Gy TBI on day 14. Group 4 (6 Gy-Irradiated): were exposed to 6 Gy TBI on day 14. Group 5 (ACE + 4 Gy): were treated with 1000 mg/Kg b.wt of ACE once daily for twenty-eight days but exposed to 4 Gy TBI on day 14. Group 6 (ACE + 6 Gy): were treated with 1000 mg/Kg b.wt of ACE once daily for twenty-eight days but exposed to 6 Gy TBI on day 14. All the groups received distilled water and feed *ad libitum* during the acclimatization and experimental periods. Four animals in each group were sacrificed 24 h after irradiation and the 4 remaining animals were sacrificed on day 29 for biochemical assay and histopathological evaluation, the statistical analysis was done using one-way analysis of variance (ANOVA) on the data editor SPSS version 28. **Results:** From the biochemical enzymes, the level of Malondialdehyde (MDA) in group 2 when compared to group 1 was almost the same, which was not statically significant with ($p > 0.05$), but groups 3 and 4 show a significant increase in the level of MDA with ($p < 0.05$) while group 5 and 6

showed no significant increase in MAD with ($p > 0.05$). The other enzymes like SOD, CAT, GST, and GSH followed suit. **Conclusion:** From the results it is a clear indication that Allium Cepa Extract can ameliorate the effect of radiation induced disease.

Keywords

Allium Cepa, Winstar RAT, MDA, SOD, Hepatoxicity

1. Introduction

Allium cepa Linn (Onion) is a valuable vegetable/field crop cultivated for food, medicine, spices and condiments worldwide since times [1]. As a vegetable crop, it ranked the second most widely cultivated after tomato production [2]. Allium cepa is a vegetable consumed worldwide; it is also a rich source of phytochemicals and organo sulphur dietary compounds that are considered to possess antioxidant properties and can also enhance systemic detoxification [3]. One of the major interests in the field of radiation biology and chemistry studies is the identification of the chemical agents that are highly potent in the protection of humans from the hazardous effect of ionizing radiation. Hence, this has lead to the study and use of plants and natural products that has the ability to offer protection against these radiation induced damage. These natural plants are less toxic in most cases or even practically non toxic compared to synthetic compounds. Some literature has been on the radio protection of Allium Cepa on an exposed rat. A study was done on the Antioxidant and the ameliorating effect of *Allium cepa* (Onion) fortified feed against potassium bromated-induced oxidative damage in Wistar rats and concluded that, in rat kidney and liver cells, potassium bromate caused oxidative damage, as evidenced by increased MDA levels and other biochemical changes. The antioxidant and ameliorative effects of the fortified feed were also demonstrated in the study, which could be attributed to the antioxidant principles contained in *Allium cepa*. [4]. While another study was done on the Radiation protection and anti-oxidative effects of garlic, onion and ginger extracts, x-ray exposed albino rats as model for biochemical studies and concluded that The comparative effects of garlic, ginger and onions on some biochemical parameters in organs of x-ray exposed rats. Changes in the body weight and organ/body weight ratio as observed in the X-ray exposed rats are indicative of X-ray toxicity. The study further showed that garlic, ginger and onion contain bioactive substances, which are radioprotective further consolidating garlic and onion with more radio-protective and anti-oxidative properties than ginger. The results indicate these plants could exert these functions through modulation in activity of several metabolizing enzymes that activate and detoxify (SOD, ALT, AO and SO), carcinogens and inhibit DNA adduct formation. Most of these enzymes have antioxidative and free radicals scavenging properties thus, involved in regulation of cell proliferation, apoptosis and immune responses.

[5]. Another study was done on the Antioxidant Effects of *Allium cepa* and Cinnamon on Sex Hormones and Serum Antioxidant Capacity in Female Rats Exposed to Power Frequency Electric and Magnetic Fields and concluded that Power frequency electromagnetic field could adversely affect sex hormones and total antioxidant capacity levels in exposed rats and *Allium cepa* and cinnamon could manuscript as an effective pharmacological supplement to moderate exposure degenerative effects [6]. Another study was done on Phytochemical screening and evaluation of antioxidant capacities of *Allium cepa*, *Allium sativum*, and *Monodora myristica* using *in vitro* and *in vivo* models and they concluded that the antioxidant activity of *A. sativum*, *M. myristica* and *A. cepa* were investigated in this study, and the outcomes showed that these food condiments are rich in antioxidants as they were able to reduce the level of ROS as well as increase the level of endogenous antioxidants. Interestingly, the *in vitro* antioxidant activity of the three food condiments was higher than that of ascorbic acid—a standard antioxidant agent. This suggests that the inclusion of these food condiments in our diet during food preparation may ameliorate oxidative stress and reduce the incidence of degenerative disease in animals. Although results from animal studies cannot be extrapolated directly to humans, further studies need to be done on the standard of dosage to minimize any adverse side effects. [7]

This study is designed to evaluate the radioprotective potential of Allium cepa (ACE) in renal tissues of winstar rats with ACE pre & post total body irradiation (TBI) of graded doses. Before now other studies has not gone to the level of studying the renal tissue of the rats rather the general kidney system is studied.

2. Materials and Method

2.1. Experimental Animal

The animals were housed in standard rat cages and left to acclimatize to laboratory condition for two weeks. The laboratory animals were kept at room temperature with access to water in accordance with the international guide for the care and use of laboratory animals (Committee for update of the guide for the care and use of laboratory animals, 2011).

2.2. Animal Strain and Number

Winstar strain and they are 60 in number.

2.3. Ace Dose Selection

ACE were administer orally to the winstar rats in three varying doses (250, 500, 1000 mg/Kg) body weight. But for the sake of this study we concentrate only on the 1000 mg/Kg b.wt.

2.4. Plant Material

Fresh onions (*Allium cepa*) were sourced locally in the market.

2.5. Preparation of Extract

Fresh bulbs of onions were carefully dressed and frozen at +4˚C. About 100 ml of chilled distilled water were added to 100 g of each of onion and crushed in a homogenizer. The resultant slurry was squeezed and filtered through a fine cloth and the filtrates of garlic, onion and ginger extracts were quickly frozen at −20˚C until used

2.6. Treatment of Animal

The animal were divided into 6 groups as earlier mentioned and each of the groups from 1 to 6 were treated adequately with what is meant for the group except the group 1 which is the control group that received only Feed and distilled water. During this treatment, rats in test groups were exposed to X-ray. The control group received nothing except food and water and they were not exposed to X-ray. The initial and final weights of the rats in each group were also recorded.

2.7. Unth Radiation and Clinnical Oncology Ethics Committee on Postgraduate Research

Approved the use of ionization radiation on winstar rats in accordance to international protocol on use of animals for research.

2.8. Radiation Dosage

The experimental albino rats (winstar strain) except those in the control group were exposed to the effect of ionization radiation from X-ray of 4 Gy and 6 Gy doses.

2.9. No of Animal Repeatedly Tested

3 animals each were tested repeatedly pergroup.

2.10. Sample Collection

At the end of the treatment period each rat was anaesthetized in chloroform saturated chamber, the rat, carefully dissected. The kidney and blood of each rat were collected and stored at −20˚C until required. The blood was collected directly from the heart using sterilized needle and syringe into well labeled heparinized containers.

2.11. Preparation of Tissue Homogenate

Ten percent homogenate of the organ was prepared in pre-chilled pestle and mortar using 4 ml, 1 − *x* ice-cold phosphate buffersaline (PBS) solution (137 mM NaCl, 10 mM phosphate, 2.7 mM KCl pH 7.4). The homogenate was centrifuge at 5000 g for 10 minutes and the supernatant obtained were used for biochemical analysis. Also blood in the heparinized container was centrifuged at 3000 g for 10 minutes after which it was separated into plasma and red cells. The

plasma at the top was pipetted carefully without the red portion into well labeled clean containers for estimation of the creatinine level present and enzyme analysis. 3 different samples where repeatedly tested per group in other to ascertain the authenticity and reliability of the results

2.12. Enzymes Assays

Different enzymes including MDA, SOD, CAT, GST, and GSH, using [8] methods, the enzymes activities, were assayed.

2.13. Stastical Analysis

The significance of the difference between ACE-treated and control group was tested by one-way analysis of variance (ANOVA). All data were represented as arithmetic mean ± standard error. The level of significance for all the results was accepted at $p < 0.05$.

3. Results

Table 1 presented the Variation in MDA and GSH levels as well as SOD, CAT and GST activities in the renal tissues of wistar rats in the various groups, with or without ACE treatment for 14 days before irradiation, while Table 2 Variation in creatinine, urea and cystatin C levels of wistar rats in the various groups, with or without ACE treatment for 14 days before irradiation. Table 3 presented the Variation in MDA and GSH levels as well as SOD, CAT and GST activities in the renal tissues of wistar rats in the various groups, with or without ACE treatment for 14 days after irradiation. While Table 4 Variation in creatinine, urea and cystatin C levels of wistar rats in the various groups, with or without ACE treatment for 14 days after irradiation. Table 5 presented the Variation in MDA and GSH levels as well as SOD, CAT and GST activities in the renal tissues of wistar rats in the various groups, with or without ACE treatment for 14 days before and after irradiation. While Table 6 Variation in creatinine, urea and cystatin C levels of wistar rats in the various groups, with or without ACE treatment for 14 days before and after irradiation. Results were reported as mean ± standard deviation.

Table 1. Variation in MDA and GSH levels as well as SOD, CAT and GST activities in the renal tissues of wistar rats in the various groups, with or without ACE treatment for 14 days before irradiation.

Groups	Doses mg/Kg b.wt	MDA (nmol/g tissue)	GSH (µmol/g tissue)	SOD (µg/g tissue)	CAT (mmol/g tissue)	GST (µmol/g tissue)
Control	-	181.58 ± 1.57	0.177 ± 0.006	104.63 ± 2.01	82.11 ± 0.58	258.62 ± 3.17
ACE	1000	156.78 ± 1.27	0.190 ± 0.006	107.79 ± 1.67	89.67 ± 0.59	267.08 ± 4.11
IRR (4 Gy)	-	307.43 ± 4.09	0.079 ± 0.003	48.16 ± 0.23	44.51 ± 0.37	146.55 ± 2.18
IRR (6 Gy)	-	362.83 ± 4.17	0.073 ± 0.005	35.86 ± 0.19	37.49 ± 0.41	139.89 ± 1.98
ACE + IRR (4 Gy)	1000	211.56 ± 1.93	0.111 ± 0.005	79.66 ± 0.47	53.31 ± 0.47	184.48 ± 2.08
ACE + IRR (6 Gy)	1000	249.43 ± 2.67	0.089 ± 0.004	64.77 ± 0.47	50.47 ± 0.45	180.35 ± 2.11

Table 2. Variation in creatinine, urea and cystatin C levels of wistar rats in the various groups, with or without ACE treatment for 14 days before irradiation.

Groups	Doses (mg/Kg b.wt)	Creatinine (mg/dL)	Urea (mg/dL)	CystatinC (µg/mL)
Control	-	0.767 ± 0.021	31.37 ± 0.18	0.818 ± 0.018
ACE	1000	0.751 ± 0.018	28.89 ± 0.13	0.796 ± 0.023
IRR (4 GY)	-	4.217 ± 0.206	73.07 ± 0.23	2.963 ± 0.144
IRR (6 GY)	-	4.636 ± 0.217	81.72 ± 0.42	3.437 ± 0.121
ACE + IRR (4 GY)	1000	1.331 ± 0.093	40.24 ± 0.19	1.207 ± 0.071
ACE + IRR (6 GY)	1000	1.519 ± 0.091	42.36 ± 0.21	1.315 ± 0.072

Table 3. Variation in MDA and GSH levels as well as SOD, CAT and GST activities in the renal tissues of wistar rats in the various groups, with or without ACE treatment for 14 days after irradiation.

Groups	Doses mg/Kg b.wt	MDA (nmol/g tissue)	GSH (µmol/g tissue)	SOD (µg/g tissue)	CAT (mmol/g tissue)	GST (µmol/g tissue)
Control	-	181.58 ± 1.57	0.177 ± 0.006	104.63 ± 2.01	82.11 ± 0.58	258.62 ± 3.17
ACE	1000	156.78 ± 1.27	0.190 ± 0.006	107.79 ± 1.67	89.67 ± 0.59	267.08 ± 4.11
IRR (4 Gy)	-	307.43 ± 4.09	0.079 ± 0.003	48.16 ± 0.23	44.51 ± 0.37	146.55 ± 2.18
IRR (6 Gy)	-	362.83 ± 4.17	0.073 ± 0.005	35.86 ± 0.19	37.49 ± 0.41	139.89 ± 1.98
ACE + IRR (4 Gy)	1000	211.56 ± 1.93	0.111 ± 0.005	79.66 ± 0.47	53.31 ± 0.47	184.48 ± 2.08
ACE + IRR (6 Gy)	1000	249.43 ± 2.67	0.089 ± 0.004	64.77 ± 0.47	50.47 ± 0.45	180.35 ± 2.11

Table 4. Variation in creatinine, urea and cysC levels of wistar rats in the various groups, with or without ACE treatment for 14 days after irradiation.

Groups	Doses (mg/Kg b.wt)	Creatinine (mg/dL)	Urea (mg/dL)	Cystatin C (µg/mL)
Control	-	0.786 ± 0.014	32.29 ± 0.24	0.823 ± 0.013
ACE	1000	0.753 ± 0.014	27.46 ± 0.21	0.794 ± 0.011
IRR (4 Gy)	-	4.309 ± 0.212	76.21 ± 0.33	2.963 ± 0.121
IRR (6 Gy)	-	4.717 ± 0.189	87.15 ± 0.41	3.437 ± 0.137
ACE + IRR (4 Gy)	1000	2.289 ± 0.156	48.71 ± 0.29	1.608 ± 0.059
ACE + IRR (4 Gy)	1000	2.471 ± 0.149	53.11 ± 0.33	1.877 ± 0.088

Table 5. Variation in MDA and GSH levels as well as SOD, CAT and GST activities in the renal tissues of wistar rats in the various groups, with or without ACE treatment for 14 days before irradiation and 14 days after irradiation.

Groups	Doses mg/Kg b.wt	MDA (nmol/g tissue)	GSH (µmol/g tissue)	SOD (µg/g tissue)	CAT (mmol/g tissue)	GST (µmol/g tissue)
Control	-	181.58 ± 1.57	0.177 ± 0.006	104.63 ± 2.01	82.11 ± 0.58	258.62 ± 3.17
ACE	1000	156.78 ± 1.27	0.190 ± 0.006	107.79 ± 1.67	89.67 ± 0.59	267.08 ± 4.11
IRR (4 Gy)	-	307.43 ± 4.09	0.079 ± 0.003	48.16 ± 0.23	44.51 ± 0.37	146.55 ± 2.18
IRR (6 Gy)	-	362.83 ± 4.17	0.073 ± 0.005	35.86 ± 0.19	37.49 ± 0.41	139.89 ± 1.98
ACE + IRR (4 Gy)	1000	191.62 ± 1.76	0.159 ± 0.014	95.53 ± 0.51	69.51 ± 0.52	241.46 ± 3.16
ACE + IRR (6 Gy)	1000	197.46 ± 1.77	0.151 ± 0.011	92.35 ± 0.51	65.27 ± 0.44	236.47 ± 2.15

Table 6. Variation in creatinine, urea and cysC levels of wistar rats in the various groups, with or without ACE treatment for 14 days before irradiation and 14 days after irradiation.

Groups	Doses (mg/Kg b.wt)	Creatinine (mg/dL)	Urea (mg/dL)	CystatinC (μg/mL)
Control	-	0.786 ± 0.014	32.29 ± 0.24	0.823 ± 0.013
ACE	1000	0.753 ± 0.014	27.46 ± 0.21	0.794 ± 0.011
IRR (4 Gy)	-	4.309 ± 0.212	76.21 ± 0.33	2.963 ± 0.121
IRR (6 Gy)	-	4.717 ± 0.189	87.15 ± 0.41	3.437 ± 0.137
ACE + IRR (4 Gy)	1000	1.132 ± 0.073	32.78 ± 0.29	1.118 ± 0.093
ACE + IRR (6 Gy)	1000	1.273 ± 0.077	33.56 ± 0.29	1.223 ± 0.091

From Figure 1, it is showed that the group that was irradiated with 4 Gy and 6 Gy showed high level of Malondialdehyde (MDA) in their renal tissue when compared with the controlled group while the group that received ACE and irradiation (*i.e.* ACE + RR (4 Gy) and ACE + IRR (6 GY)) has almost the same level of MDA with the control group at $p < 0.001$.

A careful observation of the figure (Figure 2) shows that the level of GSH in control and ACE group is high when compared to the irradiated groups (*i.e.* IRR 6 Gy and IRR 4 Gy), while the group ACE + IRR (4 Gy) and ACE + IRR (6 Gy) show significant increase from (IRR 6 Gy and IRR 4 Gy) at $p < 0.001$.

The figure (Figure 3) shows that the level of SOD in the ACE and control group is very high when compare to the irradiated group (*i.e.* IRR (4 Gy) and IRR (6 Gy)) from the careful observation of the above figure. The other group which is ACE + IRR for both 6 Gy and 4 Gy shows a significant increase from IRR groups at $p < 0.00001$.

From the figure (Figure 4), there is a decrease in the level of CAT in IRR (4 Gy) and IRR (6 Gy) groups when compared to the ACE and the control group. While ACE + IRR (4 Gy) and ACE + IRR (6 Gy) group shows a significant increment from the irradiated group at $p > 0.01$.

The level of GST from the figure (Figure 5) in the irradiated group (*i.e.* IRR 4 Gy and IRR 6 Gy) decrease significantly when compared to the level in control and ACE group, while ACE + IRR 4 Gy and ACE + IRR 6 Gy show an increment in level from the irradiated group at $p < 0.0001$.

The level of serum creatinine is high in the irradiated group when compared with control group. The other group which is ACE + IRR 6 Gy and ACE + IRR 4 Gy had an insignificant increment when compared with control at $p < 0.0001$. Please see Figure 6.

The level of serum urea is high in the irradiated group when compared with control group. The other group which is ACE + IRR 6 Gy and ACE + IRR 4 Gy had an insignificant increment when compared with control at $p < 0.001$. Please see Figure 7.

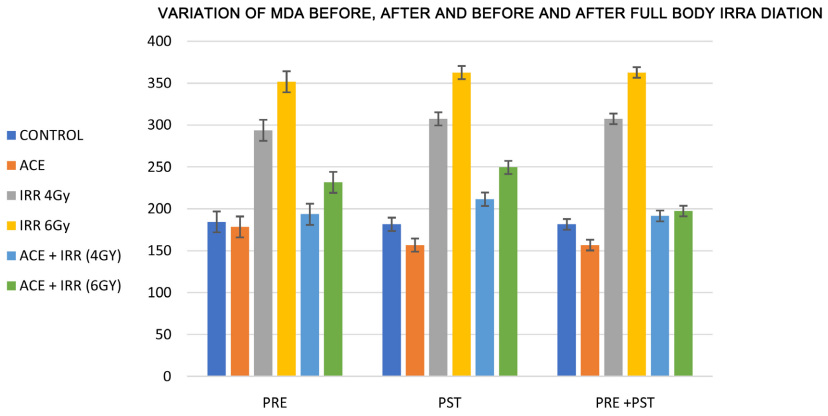

Figure 1. Malondialdehyde (MDA) concentration in the kidney of the various groups with or without administration of 1000 mg/Kg b.wt of ACE before, after or before and after exposure to graded doses of radiation of 4 Gy or 6 Gy (with significant level at $p < 0.001$).

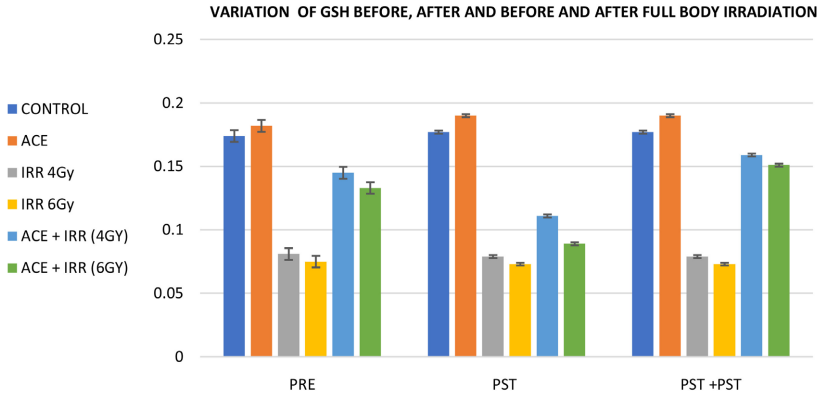

Figure 2. Glutathione (GSH) concentration in the kidney of the various groups with or without administration of 1000 mg/Kg b.wt of ACE before, after or before and after exposure to graded doses of radiation of 4 Gy or 6 Gy (at a significant level of $p < 0.001$).

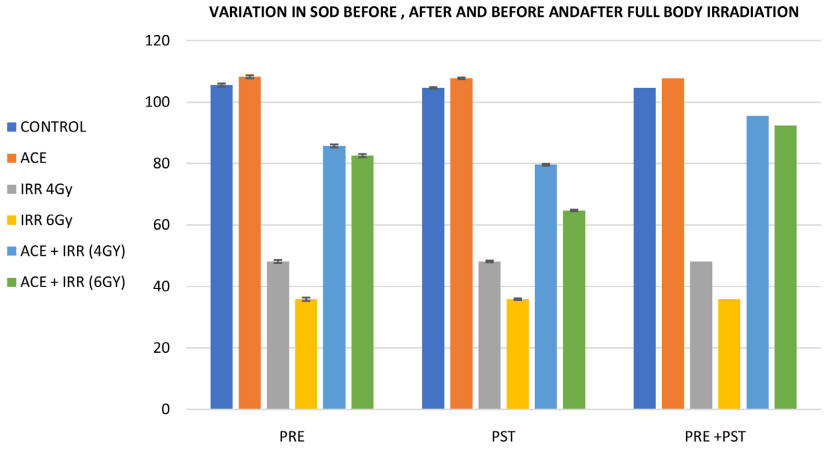

Figure 3. Activities of superoxide dismutase (SOD) in the kidney of the rats in the various groups with or without administration of 1000 mg/Kg b.wt of ACE before, after or before and after exposure to graded doses of radiation of 4 Gy or 6 Gy (at a significant level of $p < 0.0001$).

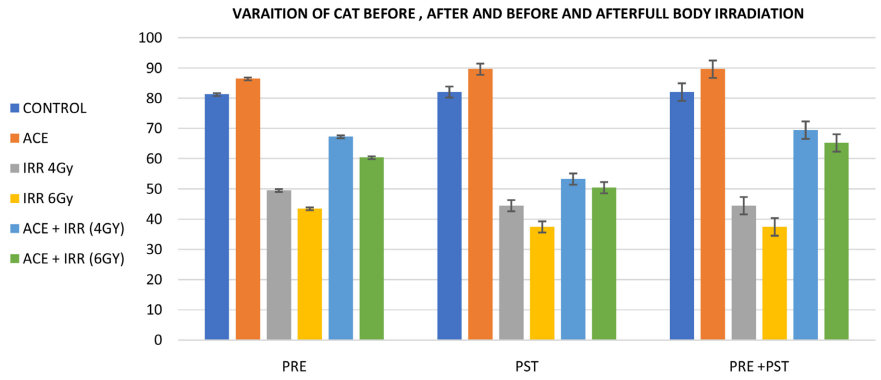

Figure 4. Activities of the catalase (CAT) concentration in the kidney of the various groups with or without administration of 1000 mg/Kg b.wt of ACE before, after or before and after exposure to graded doses of radiation (at a significant level of $p > 0.01$).

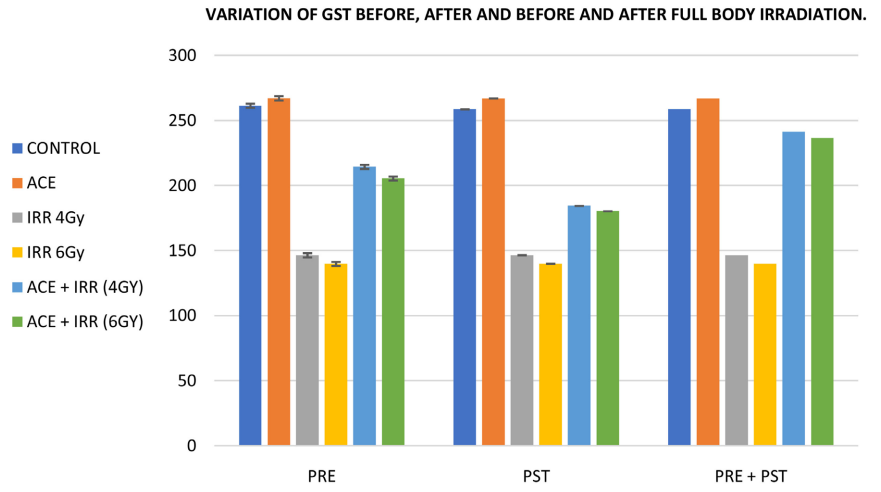

Figure 5. Activities of glutathione-S-transferase (GST) in the kidney of the various groups with or without administration of 1000 mg/Kg b.wt of ACE before, after, before and after exposure to graded doses of radiation of 4 Gy or 6 Gy (at a significant level of $p < 0.0001$).

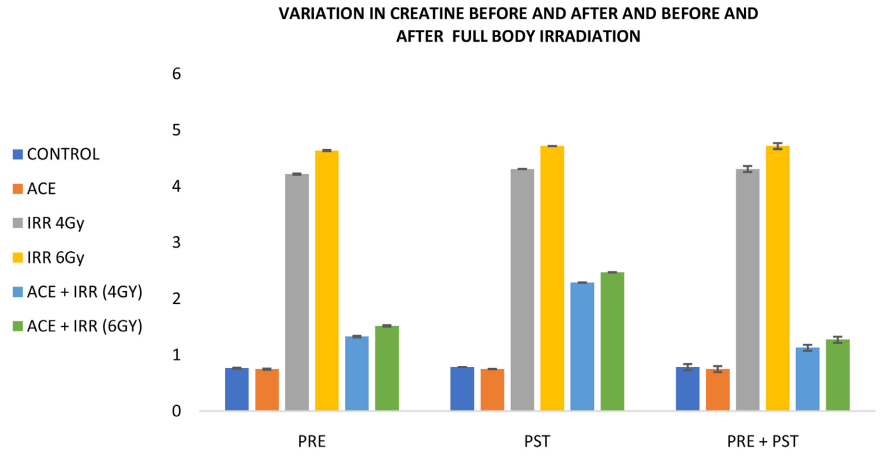

Figure 6. Serum creatinine concentration in the various groups with or without administration of 1000 mg/Kg b.wt of ACE (at a significant level of $p < 0.0001$).

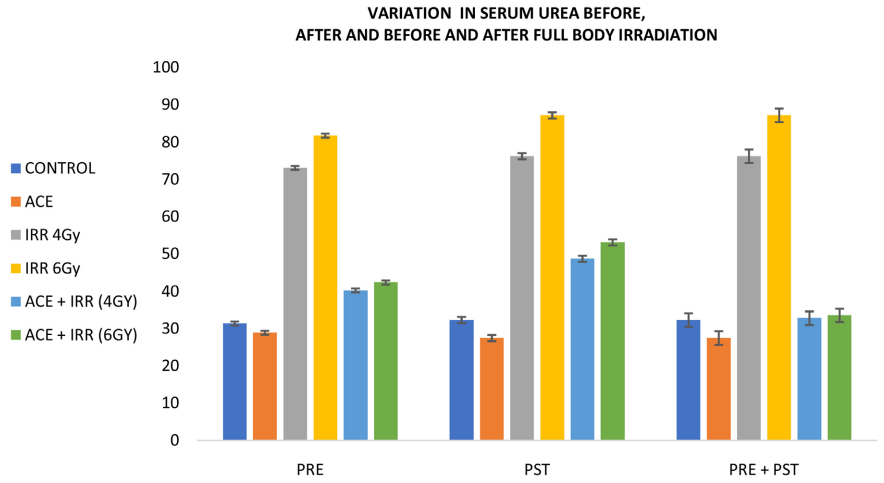

Figure 7. Serum urea concentration in the various groups with or without administration of 1000 mg/b.wt of ACE before, after or before and after exposure to graded doses of radiation of 4 Gy or 6 Gy (at a significant level of $p < 0.001$).

The level of serum Cystatin is high in the irradiated group when compared to the control group. The other group which is ACE + IRR 6 Gy and ACE + IRR 4 Gy had an insignificant increment when compared with control at $p < 0.05$. Please see **Figure 8**.

3.1. Malondialdehyde (MDA)

Malondialdehyde (MDA): MDA is widely used as a biomarker for assessing oxidative stress in biomedical fields. Lipid peroxidation is a chain phenomenon resulting in the formation of various active compounds that result in cellular damage. Determination of MDA in blood plasma or tissue homogenates is one of the useful methods to predict the oxidative stress levels [8]. They suggested that increase in the level of MDA is an indication of oxidative stress.

14 DAYS BEFORE IRRADIATION (PRE).

From **Figure 1**, It is observed that there is an insignificant decrease in the level of MDA immediately the rats were administered ACE 14 days before irradiation from its level in the control group which is not statistically significant with ($p > 0.05$) in order of 3% (184.51 ± 3.37 Vs 178.53 ± 2.59). The level of MDA increased significantly in group irradiated with 4 Gy with ($p < 0.05$) in order of 59% (184.51 ± 3.37 Vs 293.72 ± 4.86), likewise in the group that was irradiated with 6 Gy a significant increase was also observed with ($p < 0.05$) in the order of 90% (184.51 ± 2.11 Vs 351.83 ± 5.03). This high increase in the level of MDA after irradiation is in accordance with the earlier study of [9]. When the rats are administered with ACE and also irradiated it is observed that the level of MDA is almost the same with the control with ($p > 0.05$) in both 4 Gy and 6 Gy groups which further prove the effectiveness of ACE as a radioprotective agent. There was a 5% increment in the level of MDA in ACE + 4 Gy group from the controlled group and 26% increment in the level of MDA in ACE + 6 Gy from the control group.

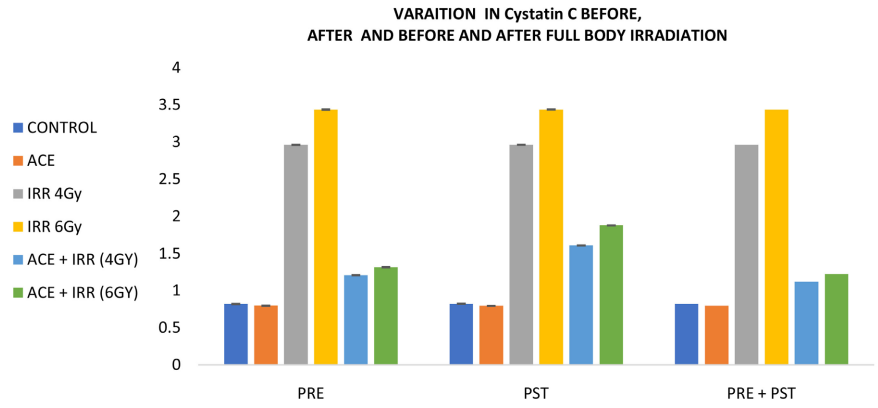

Figure 8. Serum Cystatin C (cysc) concentration in the various groups with or without administration of 1000 mg/Kg b.wt of ACE before, after or before and after exposure to graded doses of radiation of 4 Gy or 6 Gy (at a significant level of $p < 0.05$).

14 DAYS AFTER IRRADIATION (POST).

The level of MDA in the renal tissue slightly reduced immediately the rats is administered ACE 14 days after irradiation from its level in the control group which is not a significant decrement with ($p < 0.05$) in order of 13% (181.58 ± 1.89 Vs 156.78 ± 1.27). This rate was increased significantly in group irradiated with 4 Gy with ($p < 0.05$) in order of 70% (181.58 ± 1.89 Vs 307.43 ± 4.09), likewise in the group that was irradiated with 6 Gy a significant increase was also observed with ($p < 0.05$) in the order of 100% (181.58 ± 1.03 Vs 362.83 ± 4.17). When the rats are administered with ACE and also irradiated it is observed that the level of MDA increased with respect to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups. There was a 17% increase in the level of MDA in ACE + 4 Gy group from the controlled group and 38% increase in the level of MDA in ACE + 6 Gy from the control group.

14 DAYS BEFORE AND AFTER IRRADIATION

The administration of ACE 14 days before and after irradiation slightly decrease the level of MDA in the renal tissue of the rats from its level in the control group which is not significant decrease with ($p < 0.05$) in order of 14% (181.58 ± 1.89 Vs 156.78 ± 1.27). This rate was increased significantly in group irradiated with 4 Gy with ($p > 0.05$) in order of 69% (181.58 ± 1.89 Vs 307.43 ± 4.09), likewise in the group that was irradiated with 6 Gy a significant increase was also observed with ($p > 0.05$) in the order of 100% (181.58 ± 1.03 Vs 362.83 ± 4.17). When the rats are administered with ACE and also irradiated it is observed that the level of MDA is almost the same with the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups. There was a 6% increment in the level of MDA in ACE + 4 Gy group from the controlled group and 9% increment in the level of MDA in ACE + 6 Gy from the control group.

3.2. Glutathione (GSH)

Glutathione (GSH): GSH is a carrier of an active thiol group in the form of a cysteine residue, it acts as an antioxidant either directly by interacting with reac-

tive oxygen/nitrogen species (ROS and RNS, resp.) and electrophiles or by operating as a cofactor for various enzymes [10].

14 DAYS BEFORE IRRADIATION.

From **Figure 2**, it is observed that after administering of ACE 14 day before irradiation the level of GSH in this ACE group slightly increase in the renal tissue of the rats with respect to the control group, the increment is not significant with ($p > 0.001$) in the order of 4% (0.174 ± 0.013 Vs 0.182 ± 0.013). There is a significant decrease in the level of GHS with ($p < 0.001$) in the order of 53% (0.174 ± 0.013 Vs 0.081 ± 0.006) when the rats is irradiated with 4 Gy. The group irradiated with 6 Gy also shows a significant decrease in the level of GHS with ($p < 0.001$) in the order of 57% (0.174 ± 0.013 Vs 0.075 ± 0.004). This result is in accordance with [11] [12] [13] [14], this is as a result of increased ROS formation and GSH reacts with reactive oxygen species (ROS) and is converted to GSSG that finally resulted glutathione depletion. When the rats are administered with ACE and also irradiated it is observed that the level of GHS decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement was not significant enough which is as a result of the ameliorative effect of Cepa. There was a 19% decrease in the level of GHS in ACE + 4 Gy group from the controlled and 14% decrement in the level of GHS in ACE + 6 Gy from the control group.

14 DAYS AFTER IRRADIATION

it is observed that after administering of ACE 14 day after irradiation the level of GSH in this ACE group slightly increase in the renal tissue of the rats with respect to the control group, the increment is not significant with ($p > 0.001$) in the order of 7% (0.177 ± 0.006 Vs 0.190 ± 0.006). There is a significant decrease in the level of GHS when the rats are irradiated with both 4 Gy and 6 Gy. The group irradiated with 4 Gy shows a significant decrease in the level of GHS with ($p < 0.001$) in the order of 55% (0.177 ± 0.006 Vs 0.079 ± 0.003) while the group irradiated with 6 Gy also shows a significant decrease in the level of GHS with ($p < 0.001$) in the order of 59% (0.177 ± 0.006 Vs 0.073 ± 0.005). When the rats are administered with ACE and also irradiated it is observed that the level of GHS decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is not significant. There was a 37% decrease in the level of GHS in ACE + 4 Gy group from the controlled and 48% decrement in the level of GHS in ACE + 6 Gy from the control group.

14 DAYS BEFORE AND AFTER IRRADIATION

it is observed that after administering of ACE 14 day before and after irradiation the level of GSH in this ACE group slightly increase in the renal tissue of the rats with respect to the control group, the increment is not significant with ($p > 0.001$) in the order of 7% (0.177 ± 0.006 Vs 0.190 ± 0.006). There is a significant decrease in the level of GHS when the rats are irradiated with both 4 Gy and 6 Gy. The group irradiated with 4 Gy shows a significant decrease in the level of GHS with ($p < 0.001$) in the order of 55% (0.177 ± 0.006 Vs 0.079 ± 0.003) while the group irradiated with 6 Gy also shows a significant decrease in the level of

GHS with ($p < 0.001$) in the order of 59% (0.177 ± 0.008 Vs 0.073 ± 0.005). When the rats are administered with ACE and also irradiated it is observed that the level of GHS decreased in comparison to the control with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is not significant. There was a 10% decrease in the level of GHS in ACE + 4 Gy group from the controlled and 15% decrement in the level of GHS in ACE + 6 Gy from the control group.

3.3. Superoxide Dismutase (SOD)

Many studies have revealed the importance of SOD in protection of normal tissue from the harmful effects of ionizing radiation [15]. Superoxide is produced as a by-product of oxygen metabolism and, if not regulated, causes many types of cell damage. Thus, SOD is an important antioxidant defense in nearly all living cells exposed to oxygen.

14 DAYS BEFORE IRRADIATION (PRE)

In **Figure 3**, after administration of ACE to the rats 14 days before irradiation, there was a slight increase in the level of SOD in the renal tissue of the rats when compared to the control group. The slight increment in the level of SOD in the renal tissue of ACE group was not significant enough with ($p < 0.05$) in the order of 3% (105.55 ± 1.76 Vs 108.27 ± 1.49). When the rats were irradiated with 4 Gy and 6 Gy there was a significant decrement in the level of SOD in the renal tissue of the rats, with the group of 4 Gy the decrement was significant with ($p < 0.0001$) in the order of 54% (105.55 ± 1.07 Vs 48.16 ± 0.37). The group of 6 Gy also show a significant decrease in the level of SOD in the renal tissue of the rats with ($p < 0.0001$) in the order of 66% (105.55 ± 1.07 Vs 35.86 ± 0.28). This in agreement with some pervious work like [16] [17] [18] [19], in which they suggested that Evidence of reduction in the activities of SOD due exposure to radiation which may induced organs injury via a mechanism of oxidative stress. When the rats are administered with ACE and also irradiated it is observed that the level of SOD decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decreament is not significant. There was a 19% decrease in the level of SOD in ACE + 4 Gy group from the controlled and 22% decrement in the level of SOD in ACE + 6 Gy from the control group.

14 DAYS AFTER IRRADIATION

It is observed from **Figure 3**, that after the administration of ACE to the rats 14 days after irradiation, there was a slight increase in the level of SOD in the renal tissue of the rats when compared to the control group. The slight increment in the level of SOD in the renal tissue of ACE group was not significant enough with ($p > 0.05$) in the order of 3% (104.63 ± 2.01 Vs 107.79 ± 1.67). When the rats were irradiated with 4 Gy and 6 Gy there was a significant decrement in the level of SOD in the renal tissue of the rats, with the group of 4 Gy the decrement was significant with ($p < 0.0001$) in the order of 54% (104.63 ± 2.01 Vs 48.16 ± 0.23). The group of 6 Gy also show a significant decrease in the level of SOD in the renal tissue of the rats with ($p < 0.0001$) in the order of 66% (104.63 ± 2.01 Vs 35.86 ± 0.19). When the rats are administered with ACE and

also irradiated it is observed that the level of SOD decreased in comparison to the control with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is a bit significant. There was a 24% decrease in the level of SOD in ACE + 4 Gy group from the controlled and 38% decrement in the level of SOD in ACE + 6 Gy from the control group.

14 DAYS BEFORE AND AFTER IRRRADIATION

It is observed from **Figure 3** that after the administration of ACE to the rats 14 days before and after irradiation, there was a slight increase in the level of SOD in the renal tissue of the rats when compared to the control group. The slight increment in the level of SOD in the renal tissue of ACE group was not significant enough with ($p > 0.05$) in the order of 3% (104.63 ± 2.01 Vs 107.79 ± 1.67). When the rats were irradiated with 4 Gy and 6 Gy there was a significant decrement in the level of SOD in the renal tissue of the rats, with the group of 4 Gy the decrement was significant with ($p < 0.0001$) in the order of 54% (104.63 ± 2.01 Vs 48.16 ± 0.23). The group of 6 Gy also show a significant decrease in the level of SOD in the renal tissue of the rats with ($p < 0.0001$) in the order of 68% (104.63 ± 2.01 Vs 35.86 ± 0.19). When the rats are administered with ACE and also irradiated it is observed that the level of SOD increased and also decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the increment and decrement is not significant. There was a 9% increment in the level of SOD in ACE + 4 Gy group from the controlled and 12% decrement in the level of SOD in ACE + 6 Gy from the control group.

3.4. Catalase (CAT)

Catalase has one of the highest turnover rates of all enzymes; one molecule of catalase can convert millions of molecules of hydrogen peroxide to water and oxygen per second.

Catalase, are frequently used by cells to rapidly catalyze the decomposition of hydrogen peroxide into less reactive oxygen species and water molecules [20].

14 DAYS BEFORE IRRADIATION

It can be observed from **Figure 4** that administration of ACE 14 days before irradiation slightly increases the level of CAT in the renal tissue of the rats when compared to its level in the control group. This slight increment is not significant enough with ($p < 0.05$) in the order of 6% (81.29 ± 0.59 Vs 86.48 ± 0.61). The level of CAT significantly decreases when the body was radiated with both 4 Gy and 6 Gy when compared with the control group. The increment in the 4 Gy group was significantly enough with ($p > 0.01$) in the order of 39% (81.29 ± 0.59 Vs 49.51 ± 0.39) while the increment in 6 Gy group is in the order of 47% (81.29 ± 0.45 Vs 43.49 ± 0.31) with ($p > 0.01$). These results are in accordance with those of [21] [22] [23] [24] who observed a significant decrease in CAT activity after exposure to irradiation due to the excess production of hydroxyl radicals (the most potent oxidant stimulate the lipid peroxidation process) and other reactive oxygen species. When the rats are administered with ACE and also irradiated it is observed that the level of CAT also decreased in comparison to the

controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement in 6 Gy is a bit significant while that of 4 Gy is not all that significant. There was a 10% increment in the level of CAT in ACE + 4 Gy group from the controlled and 19% decrement in the level of SOD in ACE + 6 Gy group from the control group.

14 DAYS AFTER IRRADIATION

It can be observed that administration of ACE 14 days after irradiation slightly increase the level of CAT in the renal tissue of the rats when compared to its level in the control group.

This slight increment is not significant enough with ($p > 0.05$) in the order of 9% (82.11 ± 0.58 Vs 89.67 ± 0.59). The level of CAT significantly decreases when the body was radiated with both 4 Gy and 6 Gy when compared with the control group. The increment in the 4 Gy group was significantly enough with ($p > 0.01$) in the order of 46% (82.11 ± 0.58 Vs 44.51 ± 0.37) while the increment in 6 Gy group is in the order of 55% (82.11 ± 0.58 Vs 37.49 ± 0.41) with ($p > 0.01$). When the rats are administered with ACE and also irradiated it is observed that the level of CAT also decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is a bit significant. There was a 35% increment in the level of CAT in ACE + 4 Gy group from the controlled and 39% decrement in the level of SOD in ACE + 6 Gy group from the control group.

14 DAYS BEFORE AND AFTER IRRADIATION

It can be observed that administration of ACE 14 days before and after irradiation, there is a slightly increase the level of CAT in the renal tissue of the rats when compared to its level in the control group. This slight increment is not significant enough with ($p > 0.05$) in the order of 5% (82.11 ± 0.58 Vs $.89.67 \pm 0.59$). The level of CAT significantly decreases when the body was radiated with both 4 Gy and 6 Gy when compared with the control group. The increment in the 4 Gy group was significantly enough with ($p < 0.01$) in the order of 46% (82.11 ± 0.58 Vs 44.51 ± 0.37) while the increment in 6 Gy group is in the order of 55% (82.11 ± 0.58 Vs 37.49 ± 0.41) with ($p < 0.01$). When the rats were administered with ACE and also irradiated it is observed that the level of CAT also decreased in comparison to the control with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is not significant. There was a 16% decrement in the level of CAT in ACE + 4 Gy group from the controlled and 21% decrement in the level of CAT in ACE + 6 Gy group from the control group.

3.5. Glutathione S-Transferases (GST)

This represents a major group of detoxification enzymes. All eukaryotic species possess multiple cytosolic and membrane-bound GST iso-enzymes, each of which displays distinct catalytic as well as non catalytic binding properties. It also appears probable that GST are regulated *in vivo* by reactive oxygen species (ROS).

14 DAYS BEFORE IRRADIATION

From **Figure 5** it is observed that if ACE is administered 14 days before irradiation, this will lead to a little increase in the level of GST in the renal tissue of the rats when compared to its level in the control group. The increment is very small with ($p < 0.0001$) in the order of 3% (258.62 ± 3.17 Vs 267.08 ± 4.11). When the rats where irradiated with both 4 Gy and 6 Gy there is a significant decrement in the level of GST in the renal tissue of the rats. There decrement in 4 Gy group is of the order of 43% (258.62 ± 3.17 Vs 146.55 ± 2.18) with ($p < 0.0001$) while that of 6 Gy has a significant decrease with ($p = 0.0001$) in the order of 46% (258.62 ± 3.17 Vs 139.89 ± 1.98), this was in agreement with the results of [25] [26]. When the rats are administered with ACE and also irradiated, it is observed that the level of GST also decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is not significant. There was a 7% decrement in the level of GST in ACE + 4 Gy group from the controlled and 9% decrement in the level of GST in ACE + 6 Gy group from the control group.

14 DAYS AFTER IRRADIATION.

It is observed that if ACE is administered 14 days after irradiation, this will lead to a little increase in the level of GST in the renal tissue of the rats when compared to its level in the control group. The increment is very small with ($p < 0.0001$) in the order of 3% (258.62 ± 3.18 Vs 267.08 ± 4.11). When the rats where irradiated with both 4 Gy and 6 Gy there is a significant decrement in the level of GST in the renal tissue of the rats. There decrement in 4 Gy group is of the order of 43% (258.62 ± 3.18 Vs 146.55 ± 2.18) with ($p < 0.0001$) while that of 6 Gy has a significant decrease with ($p < 0.0001$) in the order of 46% (258.62 ± 3.18 Vs 139.89 ± 1.98). When the rats are administered with ACE and also irradiated, it is observed that the level of GST also decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is a little significant. There was a 6% decrement in the level of GST in ACE + 4 Gy group from the controlled and 9% decrement in the level of GST in ACE + 6 Gy group from the control group.

14 DAYS BEFORE AND AFTER ARRADIATION.

It is observed that if ACE is administered 14 days before and after irradiation, this will lead to a little increase in the level of GST in the renal tissue of the rats when compared to its level in the control group. The increment is very small with ($p < 0.0001$) in the order of 3% (258.62 ± 3.17 Vs 267.75 ± 3.41). When the rats where irradiated with both 4 Gy and 6 Gy there is a significant decrement in the level of GST in the renal tissue of the rats. There decrement in 4 Gy group is of the order of 43% (258.62 ± 3.17 Vs 146.55 ± 2.18) with ($p < 0.0001$) while that of 6 Gy has a significant decrease with ($p < 0.0001$) in the order of 46% (258.62 ± 3.17 Vs 139.89 ± 1.98). When the rats are administered with ACE and also irradiated, it is observed that the level of GST also decreased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is not significant. There was a 7% decrement in the level of GST in ACE + 4 Gy group

from the controlled and 9% decrement in the level of GST in ACE + 6 Gy group from the control group.

3.6. Serum Creatinine

Serum creatinine (a blood measurement) is an important indicator of kidney health because it is an easily measured byproduct of muscle metabolism that is excreted unchanged by the kidneys. Creatinine itself is produced via a biological system involving creatine, phosphocreatine (also known as creatine phosphate), and adenosine triphosphate (ATP, the body's immediate energy supply) [27].

14 DAYS BEFORE IRRADIATION.

From **Figure 6** it is observed that after administering the rats with ACE 14 days before irradiation, the level creatinine in the renal tissue of the rats decreased slightly with ($p < 0.05$) in the order of 2% (0.767 ± 0.021 Vs 0.751 ± 0.018). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of creatinine in the renal tissue of the rats increase significantly. The 4 Gy group show a significant increment with ($p < 0.0001$) in the order of 451% (0.767 ± 0.021 Vs 4.217 ± 0.206) while the 6 Gy group increased with ($p < 0.0001$) in the order 504% (0.767 ± 0.021 Vs 4.636 ± 0.217). This result is in Accordance with [28], the elevation of creatinine post irradiation might be due to the back leakage of the filtered creatinine, which may occur through the damaged tubular epithelium due irradiation likewise, [28] also reported an elevation in the level of Creatinine in response to full body irradiation. When the rats are administered with ACE and also irradiated, it is observed that the level of creatinine also increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the increment is significant. There was a 74% increment in the level of creatinine in ACE + 4 Gy group from the controlled and 98% increment in the level of creatinine in ACE + 6 Gy group from the control group.

14 DAYS AFTER IRRADIATION

It is observed that after administering the rats with ACE 14 days after irradiation, the level creatinine in the renal tissue of the rats decreased slightly but the decrement was not significant enough with ($p < 0.05$) in the order of 4% (0.786 ± 0.014 Vs 0.753 ± 0.014). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of creatinine in the renal tissue of the rats increase significantly. The 4 Gy group show a significant increment with ($p < 0.0001$) in the order of 461% (0.786 ± 0.014 Vs 4.309 ± 0.212) while the 6 Gy group increased with ($p < 0.0001$) in the order 514% (0.786 ± 0.014 Vs 4.717 ± 0.189). When the rats are administered with ACE and also irradiated, it is observed that the level of creatinine also increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is not significant. There was a 191% increment in the level of creatinine in ACE + 4 Gy group from the controlled and 214% increment in the level of creatinine in ACE + 6 Gy group from the control group.

14 DAYS BEFORE AND AFTER IRRADIATION.

It is observed that after administering the rats with ACE 14 days after irradia-

tion, the level creatinine in the renal tissue of the rats decreased slightly but the decrement was not significant enough with ($p > 0.001$) in the order of 3% (0.767 ± 0.011 Vs 0.744 ± 0.014). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of creatinine in the renal tissue of the rats increase significantly. The 4 Gy group show a significant increment with ($p < 0.0001$) in the order of 461% (0.767 ± 0.001 Vs 4.309 ± 0.237) while the 6 Gy group increased with ($p < 0.0001$) in the order 514% (0.767 ± 0.001 Vs 4.717 ± 0.242). When the rats are administered with ACE—and also irradiated, it is observed that the level of creatinine also increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the increment is not significant. There was a 8% increment in the level of creatinine in ACE + 4 Gy group from the controlled and 38% increment in the level of creatinine in ACEE + 6 Gy group from the control group, which is significant

3.7. Serum Urea

Measurement of serum urea has been used for many years as an indicator of kidney function. Kidney toxicity is associated with reduced urea extraction and consequence high concentration in the blood.

14 DAYS BEFORE IRRADIATION.

From **Figure 7** it is observed that after administering the rats with ACE 14 days before irradiation, the level Urea in the renal tissue of the rats decreased significantly with ($p < 0.01$) in the order of 9% (31.37 ± 0.18 Vs 28.89 ± 0.13). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of Urea in the renal tissue of the rats increase significantly. The 4 Gy group show a significant increment with ($p < 0.001$) in the order of 132% (31.37 ± 0.18 Vs 73.07 ± 0.23) while the 6 Gy group increased with ($p < 0.01$) in the order 160% (31.37 ± 0.218 Vs 81.72 ± 0.42), this is in accordance with the works of (23) and (22). When the rats are administered with ACE and also irradiated, it is observed that the level of Urea also increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the increment is not statistically significant. There was a 29% increment in the level of Urea in ACE + 4 Gy group from the controlled and 35% increment in the level of Urea in ACE + 6 Gy group from the control group.

14 DAYS AFTER IRRADIATION

It is observed that after administering the rats with ACE 14 days before irradiation, the level Urea in the renal tissue of the rats decreased slightly but the decrement which is significant with ($p < 0.01$) in the order of 15% (32.29 ± 0.24 Vs 27.46 ± 0.21). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of Urea in the renal tissue of the rats increase significantly. The 4 Gy group show a significant increment with ($p < 0.001$) in the order of 137% (32.29 ± 0.24 Vs 76.21 ± 0.33) while the 6 Gy group increased with ($p < 0.01$) in the order 171% (32.29 ± 0.24 Vs 87.15 ± 0.41). When the rats are administered with ACE and also irradiated, it is observed that the level of Urea also increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy

groups but the decrement is not significant. There was a 50% increment in the level of Urea in ACE + 4 Gy group from the controlled and 65% increment in the level of Urea in ACE + 6 Gy group from the control group.

14 DAYS BEFORE AND AFTER IRRADIATION.

It is observed that after administering the rats with ACE 14 days before irradiation, the level Urea in the renal tissue of the rats decreased slightly but the decrement was not significant enough with ($p < 0.01$) in the order of 4% (32.29 ± 0.24 Vs 27.46 ± 0.21). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of Urea in the renal tissue of the rats increase significantly. The 4 Gy group show a significant increment with ($p < 0.01$) in the order of 137% (32.29 ± 0.24 Vs 76.21 ± 0.33) while the 6 Gy group increased with ($p < 0.001$) in the order 171% (32.29 ± 0.24 Vs 87.15 ± 0.41). When the rats are administered with ACE and also irradiated, it is observed that the level of Urea increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups. There was a 0% increment in the level of Urea in ACE + 4 Gy and 3% increment in the level of Urea in ACE + 6 Gy group.

3.8. Cystatin C

Concentrations of cystatin C are reliable markers for detecting and monitoring the progression of kidney disease [23]. Cystatin C is a protein that is produce by the cell, when the kidney is working very well it will keep the level of cystatin C right. If the level of Cystatin C is high in the blood, it is a sign that the kidney is malfunctioning.

14 DAYS BEFORE IRRADIATION.

From **Figure 8** it is observed that after administering the rats with ACE 14 days before irradiation, the level Cystatin C in the renal tissue of the rats decreased slightly but the decrement was not significant enough with ($p > 0.05$) in the order of 4% (0.818 ± 0.015 Vs 0.788 ± 0.021). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of Cystatin C in the renal tissue of the rats increase significantly, this as in accordance with the work of [24] The 4 Gy group show a significant increment with ($p < 0.05$) in the order of 262% (0.818 ± 0.015 Vs 2.963 ± 0.171) while the 6 Gy group increased with ($p < 0.05$) in the order 320% (0.818 ± 0.015 Vs 3.437 ± 0.213). When the rats are administered with ACE and also irradiated, it is observed that the level of Cystatin C also increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the increment is significant. There was a 36% increment in the level of Cystatin C in ACE + 4 Gy group from the controlled and 48% increment in the level of Cystatin C in ACE + 6 Gy group from the control group.

14 DAYS AFTER IRRADIATION

It is observed that after administering the rats with ACE 14 days before irradiation, the level Cystatin C in the renal tissue of the rats decreased slightly but the decrement was not significant enough with ($p > 0.05$) in the order of 4% (0.818 ± 0.015 Vs 0.788 ± 0.021). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of Cystatin C in the renal tissue of the rats in-

crease significantly. The 4 Gy group show a significant increment with ($p < 0.05$) in the order of 262% (0.818 ± 0.015 Vs 2.963 ± 0.171) while the 6 Gy group increased with ($p < 0.05$) in the order 320% (0.818 ± 0.015 Vs 3.437 ± 0.213). When the rats are administered with ACE and also irradiated, it is observed that the level of Cystatin C also increased in comparison to the controlled with ($p > 0.05$) in both 4 Gy and 6 Gy groups but the decrement is not significant. There was a 49% increment in the level of creatinine in ACE + 4 Gy group from the controlled and 82% increment in the level of creatinine in ACE + 6 Gy group from the control group.

14 DAYS BEFORE AND AFTER IRRADIATION.

It is observed that after administering the rats with ACE 14 days before irradiation, the level Cystatin C in the renal tissue of the rats decreased slightly but the decrement was not significant enough with ($p > 0.05$) in the order of 4% (0.818 ± 0.015 Vs 0.788 ± 0.021). When the rats where irradiated with both 4 Gy and 6 Gy, it is observed that the level of Cystatin C in the renal tissue of the rats increase significantly. The 4 Gy group show a significant increment with ($p < 0.05$) in the order of 262% (0.818 ± 0.015 Vs 2.963 ± 0.171) while the 6 Gy group increased with ($p < 0.05$) in the order 320% (0.818 ± 0.015 Vs 3.437 ± 0.213). When the rats are administered with ACE and also irradiated, it is observed that the level of Cystatin C decreased insignificantly in comparison to the controlled with ($p > 0.05$) in both 4 Gy groups but. There was a 1% decrement in the level of Cystatin C in ACE + 4 Gy group from the controlled and 11% increment in the level of Cystatine C in ACE + 6 Gy group from the control group.

4. Discussion

The ameliorating effect of the *Allium cepa* against oxidative damage induced by radiation was due to the antioxidant bioactive constituent of *Allium cepa* [29]. The ameliorating effect reported in the study could be due to the antioxidant phytochemical compound such as flavonoids and phenolics contained in the onions as was shown in this study. Previous studies reported that *Allium cepa* is rich in phenols and sulphur-containing compounds which were implicated in many health and beneficial effect [30] [31]. Malondialdehyde (MDA), is one of the most abundant carbonyl products of lipid peroxidation and biomarker of oxidative stress [32]. The free radical scavenging activity of the Allium Cepa was responsible for the reduced MDA level in all the tissues of rats; this aligns with the study of [33] which reported on high scavenging activities of onions. Increased levels of MDA and decreased levels of GSH, SOD and CAT were observed in renal tissue in the irradiated animals. Allium cepa leaves extract efficiently counteracted the radiation induced renal tissue damage by significantly decreasing the MDA levels and increasing the GSH, SOD and CAT activities. The antioxidant enzymes such as SOD and CAT constitute the major supportive team of defense against free radicals. The equilibrium between these enzymes is an important process for the effective removal of ROS in intracellular organelles

[34]. In present study, a significant decrease in levels of SOD and CAT enzymes in irradiated group was observed. Allium cepa leaves extract treatment significantly reversed the changes in antioxidant levels induced by radiation. A decrease in the activity of SOD can result in the decreased removal of superoxide ion, which can be harmful to the organs. Moreover, the enhanced SOD activity in the Allium cepa leaves extract treated group might be involved in the scavenging of O^{2-} generated from radiation.

Similarly, the increased oxidative damage by radiation was responsible for the increased SOD activity in irradiated rats, however, *Allium cepa* proffers antioxidant first line of defense against ROS in the groups administered with CEPA. The interplay between SOD, catalase and glutathione have been reported in some studies to have a protective role on SOD against the overwhelming effect of high concentration of ROS in the cell, which inhibits the activity of SOD. The decreased level of glutathione reductase in the irradiated group in this study could be due to antioxidant activity on SOD and its direct mopping of ROS in the cell [34] [35]. Radiation significantly decreased the level of tissue GSH in accordance with the previous studies [33]. Decrease in the levels of GSH represents its increased utilization by myocardial cells due to oxidative stress. Treatment with Allium cepa has significantly restored the GSH levels, this effect could be attributed either to increased biogenesis of GSH or the reduction in oxidative stress levels leading to decreased generation of toxic free-radical specie. Furthermore, increased level of glutathione reductase, in the animals administered with Allium Cepa, gave credence to the antioxidant property of *Allium cepa*. It has been known that glutathione S-transferases (GSTs) can reduce lipid hydroperoxides (LPO) through their Se-independent glutathione-peroxidase activity and that these enzymes can also detoxify LPO end-products such as 4HNE [36].

This study also showed that there was a significant reduction in the urine volume of irradiated rats. This is in consonance with previous studies and confirms that cadmium administration or exposure causes renal tubular damage, declined renal function, decrease glomerular rate (GFR) and impaired renal blood flow (RBE) [37]. Administration of ACE alleviated radiation urine volume alteration. This could suggest that ACE improves renal function by preventing renal tubular damage and enhancement of RBF and GFR.

This study also documents the effect of radiation and ACE on renal clearance. A significant decrease in urea and creatinine clearance was seen in the irradiated group of rats only when compared to all other groups. This is similar to previous studies [37]. This study suggests that the impaired renal clearance seen in the irradiated group is due to the reduced urine volume. A significant decrease in urea and creatinine clearance was also seen in ACsE-pre-treated and post-treated rats. However, this was only significant when compared to the control group, but not the other groups. Co-treatment of radiation with ACE showed no significant impairment of renal clearance. This suggests that co-treatment of radiation with ACE is most potent in preventing radiation-induced renal dysfunction by im-

proving renal clearance and urine volume than pre-treatment and post-treatment of radiation with ACE. Creatinine, a metabolic intermediate of muscle metabolism that is cleared through glomeruli of the nephron [38]. The increased serum creatinine levels in the group fed fortified feed in this study might be as a result of a transient increase induced by *Allium cepa* [39]. Furthermore, the normal architectural cells of the kidney gave credence to the protective potency of *Allium cepa* in the group treated with ACE and also irradiated as earlier stated. This may be due to the ameliorating activity of the *Allium cepa* against oxidative stress.

5. Conclusion

In rat kidney, radiation caused oxidative damage, as evidenced by increased MDA levels and other biochemical changes. The antioxidant and ameliorative effects of the Allium cepa were also demonstrated in the study, which could be attributed to the antioxidant principles contained in *Allium cepa*. Antioxidant effects of Allium cepa and its constituents were mediated through stabilization of cellular membranes, ROS scavenging, and decrement of unsaturated membrane lipids peroxidation. Therefore, Allium cepa and its constituents could be of therapeutic value in disorders such as aging induced by radiation, and wound healing processes where radical scavenging activity can be of therapeutic value. Although the exact molecular mechanisms underlying such effects are not fully understood yet, most of pharmacological activities of Allium cepa are related to the presence of bioactive compounds such as quercetin. Further clinical studies are needed to evaluate the effect of the plant and its constituents on conditions induced by oxidative stress which leads to immune-dysregulation. In addition, scientific information on toxicity or safety of onion has not been fully explored and requires further studies.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] El-Aziz, M.A., Morsi, S.M.M., Salama, D.M., Abdel-Aziz, M.S., Elwahed, M.S.A., Shaaban, E.A. and Youssef, A.M. (2019) Preparation and Characterization of Chitosan/Polyacrylic Acid/Copper Nanocomposites and Their Impact on Onion Production. *International Journal of Biological Macromolecules*, **123**, 856-865. https://doi.org/10.1016/j.ijbiomac.2018.11.155

[2] Bahram-Parvar, M. and Lim, L.T. (2018) Fresh-Cut Onion: A Review on Processing, Health Benefits, and Shelf-Life. *Comprehensive Reviews in Food Science and Food Safety*, **17**, 290-308. https://doi.org/10.1111/1541-4337.12331

[3] Jaiswal, N., Kumar, D. and Rizvi, S.I. (2013) Red Onion Extract (*Allium cepa* L.) Supplementation Improves Redox Balance in Oxidatively Stressed Rats. *Food Science and Human Wellness*, **2**, 99-104. https://doi.org/10.1016/j.fshw.2013.05.003

[4] Nwonuma, C.O., Osemwegie, O.O., Alejolowo, O.O., Irokanulo, E.O., Olaniran,

A.F., Fadugba, D.O., Opaleke, D.O. and Ojo, O.A. (2021) Antioxidant and the Ameliorating Effect of *Allium cepa* (Onion) Fortified Feed against Potassium Bromate Induced Oxidative Damage in Wistar Rats. *Toxicology Reports*, **8**, 759-776. https://doi.org/10.1016/j.toxrep.2021.03.029

[5] Kenneth, C.N., Samuel, O.A., Chibueze, N. and Michael, P.O. (2014) Radiation Protection and Anti-Oxidative Effects of Garlic, Onion and Ginger Extracts, x-Ray Exposed Albino Rats as Model for Biochemical Studies. *African Journal of Biochemistry Research*, **8**, 166-173. https://doi.org/10.5897/AJBR2014.0794

[6] Elham, M., Ahmad, K., Amir, A.K. and Arash, K. (2016) Antioxidant Effects of *Allium cepa* and Cinnamon on Sex Hormones and Serum Antioxidant Capacity in Female Rats Exposed to Power Frequency Electric and Magnetic Fields. *International Journal of Women's Health and Reproduction Sciences*, **4**, 141-145. https://doi.org/10.15296/ijwhr.2016.32

[7] Irozuru, C.E., Olugbodi, J.O., Arunsi, U.O. and Ladeji, O. (2021) Phytochemical Screening and Evaluation of Antioxidant Capacities of *Allium cepa*, *Allium sativum*, and *Monodora myristica* Using *in vitro* and *in vivo* Models. *African Research Opinion Communication in Food and Nutrition*, **1**, 41-52. https://doi.org/10.53858/arocfn01014152

[8] Armas-Padilla, M.C., Armas-Hernández, M.J., Sosa-Canache, B., Cammarata, R., Pacheco, B., Guerrero, J., Carvajal, A.R., Hernández-Hernández, R., Israili, Z.H. and Valasco, M. (2007) Nitric Oxide and Malondialdehyde in Human Hypertension. *American Journal of Therapeutics*, **14**, 172-176. https://doi.org/10.1097/01.pap.0000249914.75895.48

[9] Samahelm, I. and Tarek, D.H. (2014) Therapeutic Influence of Allium Cepa Extract on Aspartame Induced Oxidative Stress and Apoptotic Changes in Rat Kidneys. *Al-Azhar Assiut Medical Journal*, **12**, 182-212.

[10] Volodymyr, I.L. (2012) Glutathione Homeostasis and Functions: Potential Targets for Medical Interventions. *Journal of Amino Acids*, **2012**, Article ID 736837. https://doi.org/10.1155/2012/736837

[11] Pourahmad, J., Ghashang, M., Ettehadi, A.H. and Ghalandari, R. (2006) A Search for Cellular and Molecular Mechanisms Involved in Depleted Uranium (DU) Toxicity. *Environmental Toxicology*, **21**, 349-354. https://doi.org/10.1002/tox.20196

[12] Pourahmad, J., Shaki, F., Tanbakosazan, F., Ghalandari, R., Ettehadi, A.H. and Dahaghin, E. (2011) Protective Effects of Fungal β-(1→3)-D-Glucan against Oxidative Stress Cytotoxicity Induced by Depleted Uranium in Isolated Rat Hepatocytes. *Human & Experimental Toxicology*, **30**, 173-181. https://doi.org/10.1177/0960327110372643

[13] Shaki, F., Hosseini, M., Ghazi-Khansarid, M. and Pourahmad, J. (2013) Depleted Uranium Induces Disruption of Energy Homeostasis and Oxidative Stress in Isolated Rat Brain Mitochondria. *Metallomics*, **5**, 736-744. https://doi.org/10.1039/c3mt00019b

[14] Hanan, W., Esraa, K., Hany, E. and Khaled, M.A. (2019) Ameliorating Effects of Thymoquinone and N-Acetylcysteine against Uranium Induced Hepatotoxicity in Rats. *Assiut University Journal of Multidisciplinary Scientific Research*, **48**, 36-59. https://doi.org/10.21608/aunj.2019.221120

[15] Holley, A.K., Miao, L., St Clair, D.K. and St Clair, W.H. (2014) Redox-Modulated Phenomena and Radiation Therapy: The Central Role of Superoxide Dismutases. *Antioxidants & Redox Signaling*, **20**, 1567-1589. https://doi.org/10.1089/ars.2012.5000

[16] Ozgur, E., Güler, G. and Seyhan, N. (2010) Mobile Phone Radiation-Induced Free Radical Damage in the Kidney Is Inhibited by the Antioxidants N-Acetyl Cysteine and Epigallocatechin-Gallate. *International Journal of Radiation Biology*, **86**, 935-945. https://doi.org/10.3109/09553002.2010.496029

[17] Marí, M., Colell, A., Morales, A., von Montfort, C., Garcia-Ruiz, C. and Fernández-Checa, J.C. (2010) Redox Control of Kidney Function in Health and Disease. *Antioxidants & Redox Signaling*, **12**, 1295-1331. https://doi.org/10.1089/ars.2009.2634

[18] Serviddio, G., Bellanti, F. and Vendemiale, G. (2013) Free Radical Biology for Medicine: Learning from Nonalcoholic Fatty Liver Disease. *Free Radical Biology and Medicine*, **6**, 952-968. https://doi.org/10.1016/j.freeradbiomed.2013.08.174

[19] Lalhminghlui, K. and Jagetia, C.G. (2018) Evaluation of the Free-Radical Scavenging and Antioxidant Activities of Chilauni, *Schima Wallichii* Korth *in vitro*. *Future Science OA*, **4**, FSO272. https://doi.org/10.4155/fsoa-2017-0086

[20] Blokhing, O., Virolaine, E. and Fagerstedt, K.V. (2003) Antioxidant, Oxidant Damage and Oxygen Desprivation Strees: A Review. *Annals of Botany*, **91**, 179-194. https://doi.org/10.1093/aob/mcf118

[21] Suru, S.M. and Ugwu, C.E. (2015) Comparative Assessment of Onion and Garlic Extracts on Endogenous Hepatic and Renal Antioxidant Status in Rat. *Journal of Basic and Clinical Physiology and Pharmacology*, **26**, 347-354. https://doi.org/10.1515/jbcpp-2014-0088

[22] Zigman, S., Reddan, J., Schultz, J.B. and McDaniel, T. (1996) Structural and Functional Changes in Catalase Induced by Near-UV Radiation. *Journal of Photo-Chemistry and Photobiology*, **63**, 818-824. https://doi.org/10.1111/j.1751-1097.1996.tb09637.x

[23] Wu, W., Abraham, L., Ogony, J., Matthews, R., Goldstein, G. and Ercal, N. (2008) Effects of Nacetylcysteine Amide (NACA), a Thiol Antioxidant on Radiation-Induced Cytotoxicity in Chinese Hamster Ovary Cells. *Life Sciences*, **82**, 1122-1130. https://doi.org/10.1016/j.lfs.2008.03.016

[24] Ismail, N., Ismail, M., Azmi, N.H., Bakar, A., Firdaus, M., Basri, H. and Abdullah, M.A. (2016) Modulation of Hydrogen Peroxide-Induced Oxidative Stress in Human Neuronal Cell by Thymoquinone-Rich Fraction and Thymoquinone via Transcriptomic Regulation of Antioxidant and Apoptotic Signaling Genes. *Oxidative Medicine and Cellular Longevity*, **2016**, Article ID: 2528935. https://doi.org/10.1155/2016/2528935

[25] Xu, H.X., Li, C.L., Mozziconacci, O., Zhu, R.Z., Xu, Y., Tang, Y.Z., Chen, R.B., Huang, Y., Holzbeierlein, J.M., Schöneich, C., Huang, J. and Li, B. (2019) Xanthine Oxidase-Mediated Oxidative Stress Promotes Cancer Cell-Specific Apoptosis. *Free Radical Biology and Medicine*, **139**, 70-79.

[26] Alshahawey, M., Shaheen, S., Elsaid, T. and Sabri, N. (2019) Effect of Febuxostat on Oxidative Stress in Hemodialysis Patients with Endothelial Dysfunction: A Randomized, Placebo-Controlled, Double-Blinded Study. *International Urology and Nephrology*, **51**, 1649-1657.

[27] Hall, J.E. (2015) Guyton and Hall Textbook of Medical Physiology. Elsevier Health Sciences, Amsterdam. https://doi.org/10.1007/s11255-019-02243-w

[28] Sefa, K., Fatih, M.K., Selçuk. Ö., Selim, Ç. and Cuneyt, C. (2021) Protective Effects of Rutin against Deltamethrin-Induced Hepatotoxicity and Nephrotoxicity in Rats via Regulation of Oxidative Stress, Inflammation and Apoptosis. *Environmental Science and Pollution Research*, **28**, 62975-62990.

[29] El-Zainy, R.M., El-Zamzamy, F.M., Shalaby, A.O.A. and Mostafa, M.Y.A. (2014) Protective Effect of Oat Biscuits Containing Herbal Oils on Potassium Bromate Induced High Oxidative Stress Rats. *Research Journal of Agriculture and Biological Sciences*, **10**, 93-108.

[30] Bystrická, J., Musilová, J., Vollmannová, A., Timoracká, M. and Kavalcová, P. (2013) Bioactive Components of Onion (*Allium cepa* L.)—A Review. *Acta Alimentaria*, **42**, 11-22. https://doi.org/10.1556/AAlim.42.2013.1.2

[31] Gawlik-Dziki, U., Świeca, M., Dziki, D., Baraniak, B., Tomiło, J. and Czyż, Z. (2013) Quality and Antioxidant Properties of Breads Enriched with Dry Onion (*Allium cepa* L.) Skin. *Food Chemistry*, **138**, 1621-1628. https://doi.org/10.1016/j.foodchem.2012.09.151

[32] Ahmad, R., Tripathi, A.K., Tripathi, P., Singh, S., Singh, R. and Singh, R.K. (2008) Malondialdehyde and Protein Carbonyl as Biomarkers for Oxidative Stress and Disease Progression in Patients with Chronic Myeloid Leukemia. *In Vivo*, **22**, 525-528.

[33] Nuutila, A.M., Puupponen-Pimiä, R., Aarni, M. and Oksman-Caldentey, K.M. (2003) Comparison of Antioxidant Activities of Onion and Garlic Extracts by Inhibition of Lipid Peroxidation and Radical Scavenging Activity. *Food Chemistry*, **81**, 485-493. https://doi.org/10.1016/S0308-8146(02)00476-4

[34] Flores-Mateo, G., Carrillo-Santisteve, P., Elosua, R., Guallar, E., Marrugat, J., Bleys, J. and Covas, M.I. (2009) Antioxidant Enzyme Activity and Coronary Heart Disease: Meta-Analyses of Observational Studies. *American Journal of Epidemiology*, **170**, 135-147. https://doi.org/10.1093/aje/kwp112

[35] Anwar, F. and Przybylski, R. (2012) Effect of Solvents Extraction on Total Phenolics and Antioxidant Activity of Extracts from Flaxseed (*Linum usitatissimum* L.). *Acta Scientiarum Polonorum*, *Technologia Alimentaria*, **11**, 293-302.

[36] Ola-Mudathir, K.F. and Maduagwu, E.N. (2014) Antioxidanteffects of Methanol Extract of Allium Cepa Linn Oncyanide-Induced Renal Toxicity in Male Wistar Rats. *Nigerian Journal of Physiological Sciences*, **29**, 147-151.

[37] Ige, S., Salawu, E., Olaleye, S., Adeeyo, O., Badmus, J. and Adeleke, A. (2009) Onion (*Allium cepa*) Extract Prevents Cadmium Induced Renal Dysfunction. *Indian Journal of Nephrology*, **19**, 140-144.

[38] Hall, J.E. (2015) Guyton and Hall Textbook of Medical Physiology. Elsevier Health Sciences, Amsterdam.

[39] Payne, R.B. (1986) Creatinine Clearance: A Redundant Clinical Investigation. *Annals of Clinical Biochemistry*: *International Journal of Laboratory Medicine*, **23**, 243-250. https://doi.org/10.1177/000456328602300304