Neuroprotective effects of ginkgo biloba extract on brain damage induced by γ-radiation and lead acetate

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Abstract- Exposure to γ-radiation and/or lead causes numerous malfunctions in the brain. The present study was performed to investigate the possible protective effect of ginkgo biloba extract in ameliorating the biochemical changes induced in brain of rats by single exposure to 6Gy whole body γ-radiation and/or i.p. administration of lead acetate (25 mg/kg) daily for seven days. Ginkgo was orally administered in two dose levels 50 and 100 mg/kg for 7 successive days. Animals were classified into 10 groups: control, 6Gy irradiated, lead-treated, irradiated lead-treated, irradiated treated by ginkgo extract in both dose levels, lead-treated receiving ginkgo in both dose levels and irradiated lead-treated receiving ginkgo in both dose levels. Radiation and/or lead acetate increased brain oxidative stress biomarkers manifested by increased brain contents of lipid peroxides and nitric oxide parallel to depletion of reduced glutathione. In addition, brain dopamine (DA) content and lactate dehydrogenase (LDH) activity increased; whereas cholinesterase (ChE) activity decreased. Furthermore, both toxicants increased brain contents of calcium and zinc; meanwhile iron content was decreased. Administration of ginkgo biloba, in both dose levels effectively alleviated radiation- and lead-induced brain oxidative stress and restored the activities of LDH and ChE enzymes. In addition, ginkgo corrected the metabolic disturbances induced in brain by radiation and lead as reflected by lowering of DA, calcium and zinc contents parallel to increased iron content. In conclusion, ginkgo biloba extract can protect the brain against the hazards of exposure to γ-radiation and/or lead.

Index Terms- Ginkgo biloba extract, γ-radiation, lead, oxidative stress, cholinesterase, dopamine.

I. INTRODUCTION

Lead toxicity remains a major health problem that can result in life-long adverse health effects. Toxicity from lead may occur through environmental and/or occupational exposure (Baranowska-Bosiacka et al., 2012). Special attention is given to the neurotoxic effect of lead as it results in intellectual and behavioral deficits in children, including hyperactivity, deficits in fine motor function, and lower performance in intelligence tests (Winneke, 2011; Baranowska-Bosiacka et al., 2012).

The CNS is exposed to ionizing radiation in a number of clinical situations; radiotherapy remains a major treatment modality for primary and metastatic neoplasms located in the CNS (Caruso et al., 2013), and exposure of the brain and the spinal cord is often unavoidable in the radiotherapeutic management of tumors located close to the CNS such as head and neck cancers. In addition, there is an increasing application of radiation in management of other disorders of the brain as epilepsy (Régis et al., 1999). The most serious complication of brain irradiation is the damage to normal tissues, which may be encountered in 40% of the cases receiving radiotherapy in brain tumors, resulting in edema and necrosis (Kamiryo et al., 1996).

A number of studies confirmed the involvement of reactive oxygen species (ROS) in radiation and lead induced toxicities (Flora et al., 2008; Pradeep et al., 2012; Zhang et al., 2013). Hence, using antioxidants to minimize lead and radiotherapy associated toxicities to the brain might prove useful.

Extracts of *ginkgo biloba* leaves have been widely used to treat cerebrovascular insufficiency, symptoms associated with dementia as well as cognitive decline and neurosensory impairments associated with aging and senility (Tian et al., 2012; Wang et al., 2013). Several studies have reported the potential of ginkgo biloba and its constituents as antioxidants and free radical scavengers (Sener et al., 2006; Martin *et al*. 2011; Tulsulkar and Shah, 2013**).** The present study was thus performed to investigate the possible protective effect of ginkgo biloba extract in ameliorating the biochemical changes in brain of rats subjected to gamma irradiation and/or lead toxicity.

II. MATERIAL AND METHODS

Animals

Adult male Wistar rats weighing 150-200 g were used in this study. They were purchased from the National Research Centre (Giza, Egypt). Animals were housed under appropriate conditions of controlled humidity and temperature. They were fed with standard pellet chow and allowed free access to water. The study was carried out according to the guidelines of the Ethics Committee of Faculty of Pharmacy, Cairo University.

Chemicals

Ginkgo biloba extract was received as a gift from Al-Amriya Pharmaceutical Industries (Alexanderia,Egypt). It contains 24% flavone glycosides (primarily composed of quercetin, kaempferol, and isorhamnetin) and 6% terpene lactones (2.8-3.4% ginkgolides A, B, and C as well as 2.6-3.2% bilobalide). Other constituents include proanthocyanidins, glucose, rhamnose, organic acids, D-glucaric acid and ginkgolic acid.

Lead acetate was purchased from Sigma-Aldrich Chemical Co., St Louis, MO, USA. All other chemicals used were of the highest analytical grade. Kits for lactate dehydrogenase (LDH) and cholinesterase (CHE) were purchased from Stanbio Main St, Boerne (USA) and Quimica Clinica Aplicada Amposta/Tarragona (Spain), respectively.

Experimental Design

Animals were classified into 10 groups. Group 1: received 1% tween 80 p.o. for seven successive days (control). Group 2: rats were subjected to 6Gy irradiation on day 7 (Sief El-Nasr et al., 1996). Group 3: rats received lead acetate (25 mg/kg/day; Daniel et al., 2004) i.p. for 7 successive days. Group 4: received lead acetate for 7 successive days and subjected to 6Gy irradiation on day 7. Groups 5 & 6: received ginkgo biloba extract (50 or 100 mg/kg; p.o.; Dias et al., 2013) and exposed to 6Gy irradiation on day 7. Groups 7 & 8: received lead acetate with ginkgo biloba extract 50 or 100 mg/kg for 7 successive days. Groups 9 & 10 received lead acetate with ginkgo biloba extract 50 or 100 mg/kg for 7 successive days and subjected to 6 Gy irradiation on day 7.

At day 8 (24 h following exposure to irradiation), all rats were sacrificed by decapitation. Brains were rapidly isolated, homogenized in ice cold saline to prepare 20% w/v homogenate using Glass-Col1 homogeniser, Terre Haute Indiana, USA. The prepared homogenates were used for determination of brain contents of nitric oxide (NO), lipid peroxides, reduced glutathione (GSH), dopamine (DA), iron, calcium and zinc as well as brain activities of CHE and LDH.

Exposure to gamma-irradiation

Whole body γ-irradiation of rats was performed at the National Centre for Radiation Research and Technology (Cairo, Egypt) using Gamma cell-40, Caesium-137 irradiation unit manufactured by the Atomic Energy of Canada Limited (AECL). Radiation dose levels were delivered at a rate of 0.46 Gy/min.

Determination of the chosen biochemical parameters

Brain NO content was measured as total nitrate/nitrite (NO_x) using Griess reagent according to the method described by Miranda et al. (2001) and expressed as µM/g wet tissue. Brain GSH content was determined using Ellman's reagent according to the method described by Beutler et al. (1963) and expressed as mg/g wet tissue. Brain lipid peroxides were determined as thiobarbituric acid reactive substances (TBARS) using malondialdehyde (MDA) as a standard according to the method described by Mihara and Uchiyama (1978) and expressed as nmol/g wet tissue. Brain DA content was determined according to the method of Guo *et al.* (2009) and expressed as µg/g wet tissue.

Brain CHE and LDH activities were determined using commercial reagent kits and expressed as U/g wet tissue. Brain calcium, iron and zinc contents were determined using the atomic absorption technique (Subramania 1995), using SOLAR System, Unicam 939 atomic absorption spectrophotometer (UK) equipped with deuterium background corrections and expressed as µg/g wet tissue.

Statistical analysis

Data were expressed as means ± S.E. Comparisons between means of different groups were carried out using one way analysis of variance (ANOVA) followed by Tukey Kramer multiple comparisons test. A probability level of less than 0.05 was accepted as being significant in all types of statistical tests. GraphPad Software InStat (version 2) was used to carry out these statistical tests.

III. RESULTS

Exposure to radiation, lead as well as their combination increased brain NO to 375.68%, 267.78% and 315.80%, respectively as compared with that of control rats (Fig. 1).Treatment with ginkgo biloba extract in a dose of 50 mg/kg decreased brain content of NO_x to 72.16%, 81.04% and 88.30% as compared with that of the corresponding irradiated, lead-treated and irradiated lead-treated rats, respectively (Fig. 1). Similarly treatment with ginkgo biloba extract (100 mg/kg) decreased brain content of NO_x to 53.64 %, 55.38 % and 73.86% as compared with that of the corresponding irradiated, lead-treated and irradiated lead- treated rats, respectively (Fig. 1).

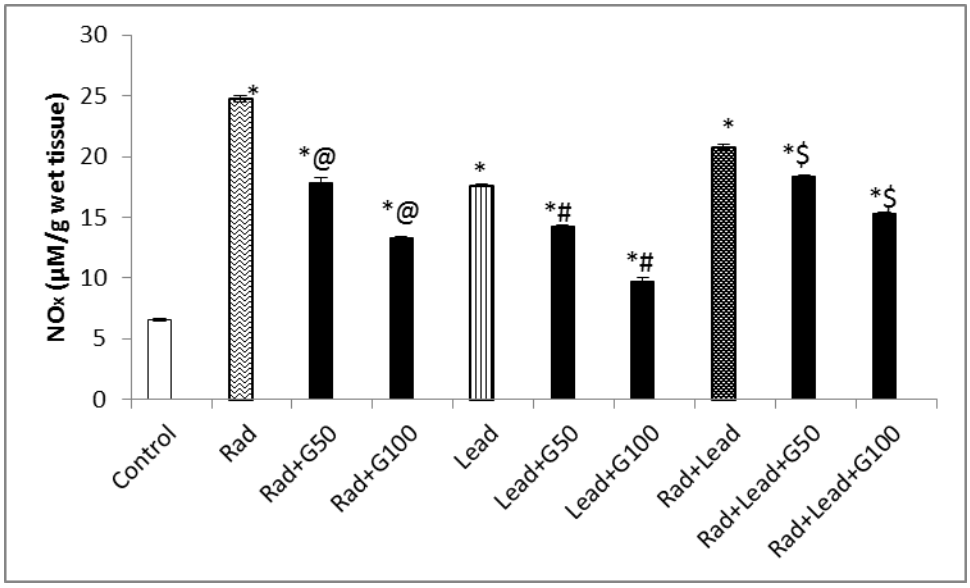

Figure (1): Effect of 7 days treatment with ginkgo biloba extract (50,100 mg/kg/day; G50, G100; p.o.) on brain content of total nitrate/nitrite (NO_x) in irradiated (Rad), lead-treated and irradiated lead-treated rats. Lead (25 mg/kg) was i.p. administered daily for seven successive days. Exposure to irradiation was done on day 7.

Results are represented as mean ± SE (n=8).
*Significantly different from control group at $p<0.05$.
@Significantly different from irradiated group at $p<0.05$.
#Significantly different from lead- treated group at $p<0.05$.
$Significantly different from irradiated lead- treated group at $p<0.05$.

Exposure to radiation, lead or their combination decreased brain GSH content to 70.57%, 52.45% and 42.82%, respectively as compared with control rats (Fig. 2). Treatment with ginkgo biloba extract (100 mg/kg) resulted in a significant increase in brain GSH content to 97.24 (137.5)%, 178.22% and 178.88% as compared with irradiated, lead-treated and irradiated lead-treated rats, respectively (Fig. 2).

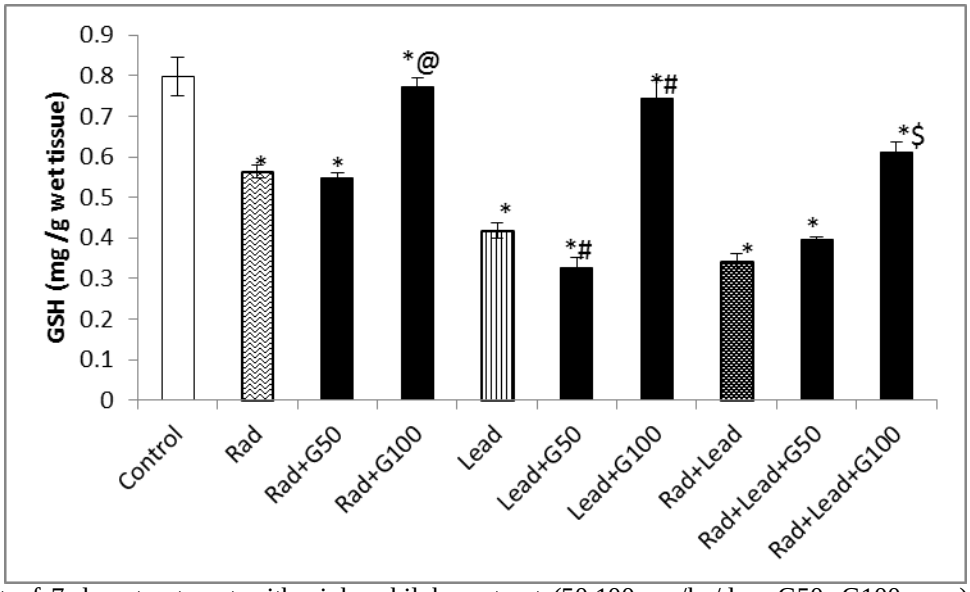

Figure (2): Effect of 7 days treatment with ginkgo biloba extract (50,100 mg/kg/day; G50, G100; p.o.) on brain content of reduced glutathione (GSH) in irradiated (Rad), lead-treated and irradiated lead-treated rats. Lead (25 mg/kg) was i.p. administered daily for 7 successive days. Exposure to irradiation was done on day 7.
Results are represented as mean ± SE (n=8).
*Significantly different from control group at $p<0.05$.
@Significantly different from irradiated group at $p<0.05$.
#Significantly different from lead- treated group at $p<0.05$.
$Significantly different from irradiated lead- treated group at $p<0.05$.

Brain lipid peroxides increased by exposure to radiation, lead or their combination to 195.47%, 248.85 % and 378.10%, respectively of the control value (Fig. 3). Treatment with ginkgo biloba extract (50 mg/kg) decreased brain content of MDA to 89.98%, 70.43% and 38.31% as compared with the corresponding irradiated, lead-treated and irradiated lead-treated values, respectively (Fig. 3). Similarly treatment with ginkgo biloba extract (100 mg/kg) decreased brain MDA content to 80.75%, 57.79% and 41.87% as compared with the corresponding irradiated, lead-treated and irradiated lead-treated values, respectively (Fig. 3).

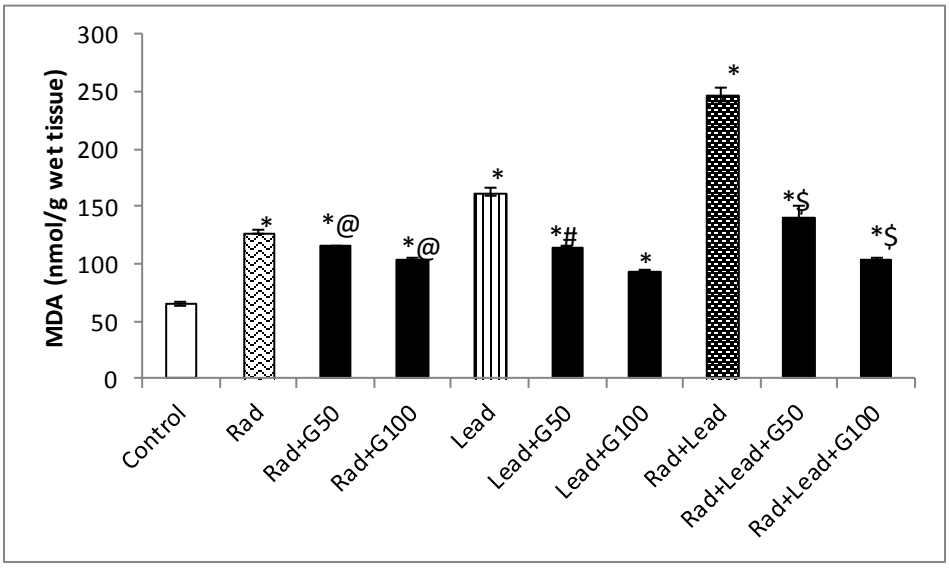

Figure (3): Effect of 7 days treatment with ginkgo biloba extract (50,100 mg/kg/day; G50, G100; p.o.) on brain content of malondialdehyde (MDA) in irradiated (Rad), lead-treated and irradiated lead-treated rats. Lead (25 mg/kg) was i.p. administered daily for 7 successive days. Exposure to irradiation was done on day 7.
Results are represented as mean ± SE (n=8).
*Significantly different from control group at $p<0.05$.
@Significantly different from irradiated group at $p<0.05$.
#Significantly different from lead- treated group at $p<0.05$.
$Significantly different from irradiated lead- treated group at $p<0.05$.

Brain LDH activity increased by exposure to radiation, lead or their combination to 206.64%, 198.54% and 233.06% as compared with the control value, respectively (Fig. 4). Treatment with ginkgo biloba extract (50 mg/kg) decreased brain LDH activity to 65.66 (79.68)%, 91.59% and 93.88% as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Fig. 4). Similarly ginkgo biloba extract (100 mg/kg) decreased brain LDH activity to 79.68% (65.66), 63.42% and 60.70% as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Fig. 4).

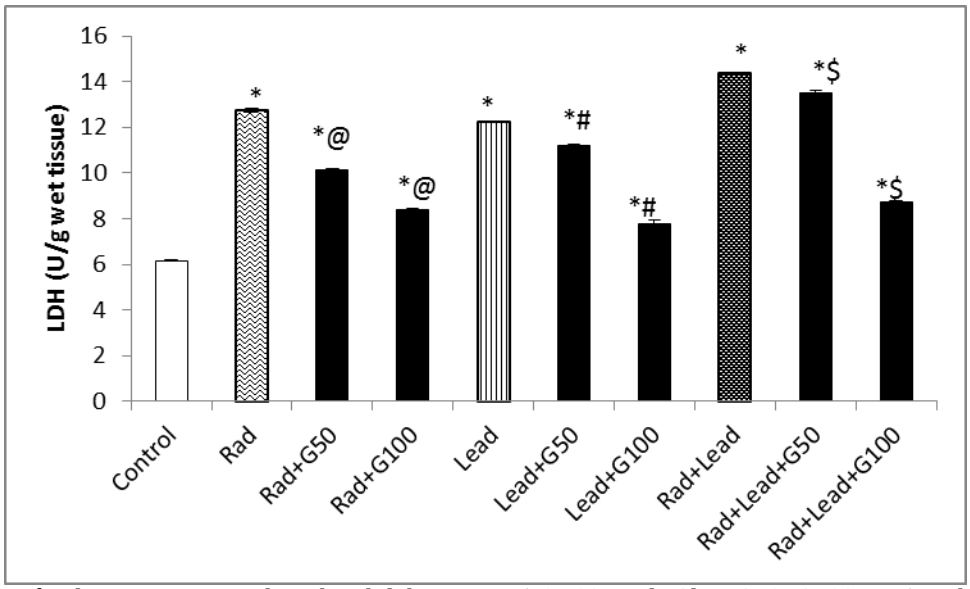

Figure (4): Effect of 7 days treatment with ginkgo biloba extract (50,100 mg/kg/day; G50, G100; p.o.) on brain activity of lactate dehydrogenase (LDH) in irradiated (Rad), lead-treated and irradiated lead-treated rats. Lead (25 mg/kg) was i.p. administered daily for 7 successive days. Exposure to irradiation was done on day 7.
Results are represented as mean ± SE (n=8).
*Significantly different from control group at $p<0.05$.

[@]Significantly different from irradiated group at $p<0.05$.
[#]Significantly different from lead- treated group at $p<0.05$.
[$]Significantly different from irradiated lead- treated group at $p<0.05$.

Exposure to radiation, lead or their combination resulted in a significant decrease in brain CHE activity of to 47.95%, 37.11% and 14.42%, respectively as compared with that of control rats (Fig. 5).Treatment with ginkgo biloba extract (100 mg/kg) increased brain CHE activity to 154.65%, 227.45% and 548.45% as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Fig. 5).

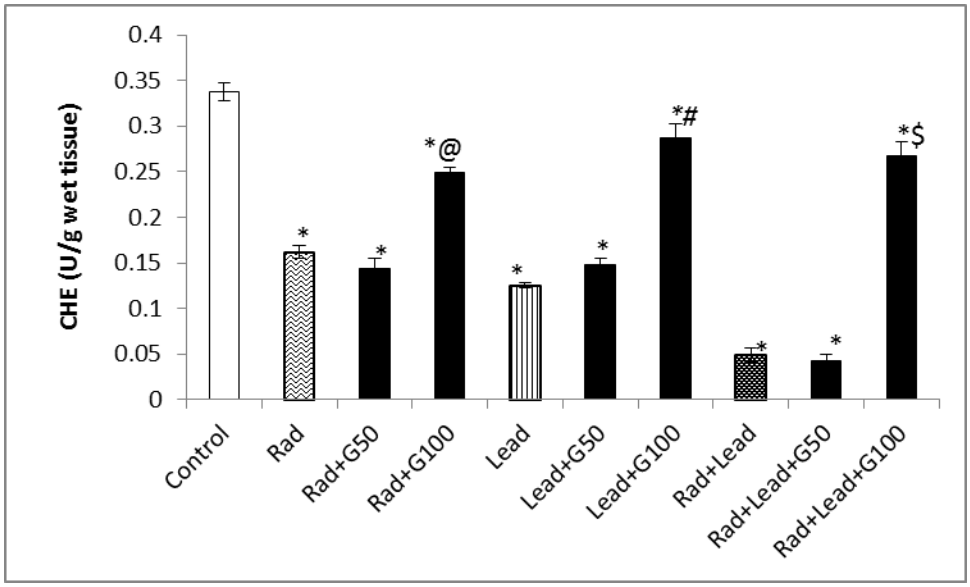

Figure (5): Effect of 7 days treatment with ginkgo biloba extract (50,100 mg/kg/day; G50, G100; p.o.) on brain activity of cholinesterase (CHE) in irradiated (Rad), lead-treated and irradiated lead-treated rats. Lead (25 mg/kg) was i.p. administered daily for 7 successive days. Exposure to irradiation was done on day 7.
Results are represented as mean ± SE (n=8).
[*]Significantly different from control group at $p<0.05$.
[@]Significantly different from irradiated group at $p<0.05$.
[#]Significantly different from lead- treated group at $p<0.05$.
[$]Significantly different from irradiated lead- treated group at $p<0.05$.

Exposure to radiation, lead or their combination resulted in significant increase brain DA content to 2656.25%, 3625.00% and 2968.75%, respectively as compared with that of control value (Fig. 6). Ginkgo biloba extract (50 mg/kg) decreased brain content of DA to 52.46%, 31.04% and 78.21% as compared with that of irradiated, lead-intoxicated and irradiated lead-intoxicated rats, respectively (Fig. 6). Similarly treatment with ginkgo biloba extract (100 mg/kg) decreased brain content of dopamine to 32.77%, 18.13% and 69.47% as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Fig. 6).

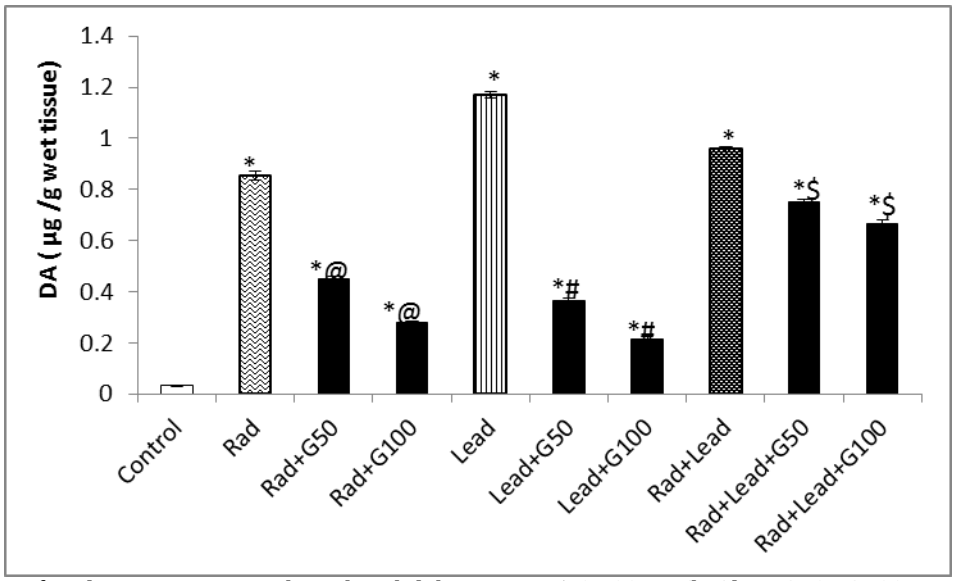

Figure (6): Effect of 7 days treatment with ginkgo biloba extract (50,100 mg/kg/day; G50, G100; p.o.) on brain content of dopamine in irradiated (Rad), lead-treated and irradiated lead-treated rats. Lead (25 mg/kg) was i.p. administered daily for 7 successive days. Exposure to irradiation was done on day 7.
Results are represented as mean ± SE (n=8).
*Significantly different from control group at $p<0.05$.
@Significantly different from irradiated group at $p<0.05$.
#Significantly different from lead- treated group at $p<0.05$.
$Significantly different from irradiated lead- treated group at $p<0.05$.

Exposure to radiation, lead or both of them increased brain calcium content to 128.80%, 210.60% and 227.30%, respectively as compared with that of control rats (Table-1). Treatment with ginkgo biloba extract (50 mg/kg) decreased brain calcium content to 89.90 %, 66.34 % and 87.00 % as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Table-1). Likewise ginkgo biloba extract (100 mg/kg) decreased brain content of calcium to 84.11%, 61.20% and 51.90% as compared with that of irradiated, lead-treated and irradiated lead-treated rats (Table-1).

Table (1): Effect of 7 days treatment with ginkgo biloba extract (G50, G100; 50, 100 mg/kg/day; p.o.) on brain content of calcium, iron and zinc in irradiated (Rad), lead- treated and irradiated lead-treated rats.

Groups	Calcium (µg/g wet tissue)	Iron (µg/g wet tissue)	Zinc (µg/g wet tissue)
Control	92.79±0.04	31.13±0.03	16.81±0.04
Rad	119.60±0.14*	20.86±0.15*	18.12±0.04*
Rad+G50	107.60±0.10*@	22.50±0.08*@	18.03±0.03*
Rad+G100	100.60±0.03*@	29.69±0.04*@	16.70±0.14*@
Lead	195.50±0.16*	22.30±0.12*	21.50±0.10*
Lead+G50	129.70±0.01*#	23.79±0.03*#	20.36±0.04*#
Lead+G100	119.80±0.03*#	27.65±0.04*#	19.43±0.01*#

Rad+ Lead	211.00±0.03*	20.73±0.11*	19.79±0.03*
Rad+ Lead+ G50	183.60±0.02$^{*\$}$	24.44±0.09$^{*\$}$	18.94±0.01$^{*\$}$
Rad+ Lead+ G100	109.70±0.10$^{*\$}$	30.40±0.01$^{*\$}$	18.11±0.03$^{*\$}$

Lead (25 mg/kg) was i.p. administered daily for seven successive days. Exposure to irradiation was done on day 7.
Results are represented as mean ± SE (n=8).
*Significantly different from control group at $p<0.05$.
$^{@}$Significantly different from irradiated group at $p<0.05$.
$^{\#}$Significantly different from lead- treated group at $p<0.05$.
$^{\$}$Significantly different from irradiated lead- treated group at $p<0.05$.

Exposure to radiation, lead or their combination decreased brain iron content to 67.00%, 71.50% and 66.59%, respectively as compared with that of control rats (Table-1). Ginkgo biloba extract (50 mg/kg) increased brain content of iron to 107.86%, 106.68% and 117.89% as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Table-1). Using ginkgo biloba extract (100 mg/kg) increased brain content of iron to 142.32%, 123.99% and 146.60% as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Table-1).

Exposure to radiation, lead or both of them increased brain content of zinc to 107.79%, 127.9% and 117.72%, respectively as compared with that of control rats (Table-1). Ginkgo biloba extract (50 mg/kg) decreased brain content of zinc to 94.69 % and 95.70% as compared with that of lead-treated and irradiated lead-treated rats, respectively (Table-1). In a similar fashion, ginkgo biloba extract (100 mg/kg) decreased brain content of zinc to 92.16%, 90.37% and 91.50% as compared with that of irradiated, lead-treated and irradiated lead-treated rats, respectively (Table-1).

IV. DISCUSSION

In the present study, single exposure to γ-radiation and/or i.p. injection of lead acetate for 7 successive days increased brain NO content that was prevented by treatment with ginkgo biloba extract in both dose levels.

Increased NO in brain of rats by lead acetate administration was previously reported (Abdel Moneim et al., 2011; Abdel Moneim, 2012; Ebuehi et al., 2012). The enhancement of NO_x content in the rat brains may be attributed to induction of inducible nitric oxide synthase (iNOS) by lead (Liu et al., 2012). In the same context, Ilhan et al. (2004) reported that exposure to electromagnetic radiation of mobile phones (900MHz for 7 days) increased brain NO content that was prevented by treatment with ginkgo biloba extract (100 mg/kg).

Single exposure to γ-radiation and/or i.p. injection of lead acetate for 7 successive days increased brain oxidative stress that was evident by increased brain lipid peroxides and reduced GSH contents. Increased oxidative stress and production of ROS following exposure to radiation (Freitinger Skalická et al., 2012; Bilgici et al., 2013) or lead intoxication (Ebuehi et al., 2012; Zhang et al., 2013**)** were previously reported. Indeed depletion of brain GSH stores following exposure to 5Gy and 6Gy whole body irradiation was reported (Manda and Bhatia, 2003). Moreover, Saxena and Flora (2006) reported than 10 weeks exposure to 0.2% lead acetate reduced brain GSH stores parallel to increased lipid peroxides formation. Increased oxidative stress indicated via depletion of glutathione (El-Ghazaly *et al.*,2013)
The brain is especially vulnerable to ROS attack owing to its high content of polyunsaturated fatty acids (PUFAs), initial targets for lipid peroxidation, and low capacity of antioxidant enzymes **(**Halliwell, 1992). This might explain brain affection by irradiation and/or lead insults and the observed protective effects of ginkgo biloba extract. The antioxidant potential of ginkgo biloba extract was previously reported in irradiated rats (Ilhan et al., 2004; Sener et al., 2006) as well as in models of hypoxia (Martin *et al*. 2011) and ischemia-reperfusion injury (Hu *et al*. 2002; Tulsulkar and Shah, 2013).

In the present study LDH activity was significantly increased in brain of rats following exposure to γ-irradiation and/or lead administration which is comparable to the results of Ivanova *et al*. (1984) and Lyshov *et al*. (1992) where enhanced LDH activity was observed in brains of rats receiving lead acetate in their drinking water. Similarly, Treshchenkova and Burlakova (1997) indicated that exposure of mice to chronic low doses of gamma radiation increased one or more of the kinetic parameters (mainly V_{max}) of LDH in the brain of mice.

The present increase in LDH activity could be explained by the findings of Popov et al. (1986) who observed an increase in the rate of glycolysis in mouse brain following exposure to whole body gamma irradiation. Furthermore, ionizing radiation was reported to cause inhibition of cellular respiration in rats (Nosov et al., 1999), this inhibition of aerobic energy production might cause the activation of anaerobic energy production and results in enhanced activity of LDH.

In the present study, ginkgo biloba extract significantly decreased brain LDH of irradiated, lead-treated and irradiated lead-treated rats. In the same context, Sener et al. (2006) showed that ginkgo (50 mg/kg) decreased brain LDH in rats exposed to whole body gamma irradiation. Brain DA content increased following whole body irradiation and/or administration of lead acetate. An increase in DA contents in cerebral cortex, hippocampus and cerebellum of rats following lead acetate administration was reported (Devi et al., 2005; Basha et al., 2012). Administration of ginkgo biloba extract reduced the

increase in brain DA content induced by irradiation or administration of lead acetate. In accordance with the present findings, Shah et al. (2003) reported that ginkgo biloba extract restored restraint stress-induced elevation in brain DA content.

In the current study, CHE activity decreased in irradiated and/ or lead-treated rats. Several other authors reported a decline in CHE activity in lead intoxicated rats (Saxena and Flora, 2006**;** Antonio-García and Massó-Gonzalez, 2008**).** In addition, Abou-Seif et al. (2003) reported a decline in brain CHE following exposure to γ-irradiation. Pretreatment of rats with ginkgo biloba extract increased brain CHE activity of irradiated or lead-treated rats. The ability of ginkgo biloba to enhance brain CHE activity, in the present study, could be the reason behinds its usefulness in dementia and Alzheimer's disease (Tian et al., 2012; Wang et al., 2013).

In the present study exposure to γ-irradiation and/or administration of lead acetate increased calcium and zinc brain contents parallel to a decrease in iron content. The present results find support in the work of Nada *et al.* (2008 & 2012) who reported an increase in zinc and calcium brain contents in rats subjected to whole body gamma irradiation (6.5 Gy). In addition, Sidhu and Nehru (2003), reported that oral administration of lead in doses of 10, 50 and 200 mg/kg for 12 weeks resulted in a significant increase in brain calcium content.

Zinc is an essential component of many metalloenzymes and is known to have several biological actions. During cell damage and inflammation, liver cells take up more Zn to synthesize nucleic acids, proteins and enzymes related to zinc (Morcillo et al., 2000; Nada et al., 2008), which could account for the observed increase in brain zinc content following irradiation or administration of lead acetate.

The increase of brain calcium content may be attributed to irradiation-induced hypoxia**;** irradiation causes ischemic cell injury associated with rushed influx of calcium from extracellular into intracellular compartment (Alden and Frith, 1991**).** Increased intracellular calcium level in rat hippocampus by lead administration was previously reported (She et al., 2009).Similarly, cerebral ischemia/reperfusion (I/R) in whole body γ-irradiated rats raised brain calcium (Ca2+) level (Abd-El-Fattah *et al.*,2010). In addition, during oxidative stress, the inadequate generation of ATP can cause malfunctioning of calcium ATPase pumps and an increase in intracellular calcium (Heunks *et al*., 1999). The latter mechanism could explain the observed effects of irradiation and lead administration on brain calcium content.

Ginkgo biloba extract attenuated changes in brain zinc, calcium and iron contents induced by irradiation and lead administration in the present study. Hu et al. (2002) reported that ginkgo biloba extract inhibited the stimulatory effect of glutamate on calcium in rats during cerebral ischemia/reperfusion. The effects of ginkgo extract on brain iron content could be mediated by induction of heme oxygenase I, which acts as an antioxidant enzyme by degrading heme into iron (Zhuang et al., 2002), hence increasing brain iron content
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V. CONCLUSION

The present study revealed the hazards of exposure to γ-radiation or lead on brain of rats. Prophylactic treatment with ginkgo biloba extract in both dose levels effectively attenuated many of the biochemical changes induced by irradiation and lead by decreasing oxidative stress, enhancing brain antioxidant status, increasing brain CHE activity and modulation of brain composition of calcium, zinc and iron.

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