ОРИГИНАЛЬНАЯ СТАТЬЯ

PROTECTIVE EVALUATION OF *ZINGIBER OFFICINALE* IN ALUMINIUM INDUCED TOXICITY IN RATS

ОЦЕНКА ПРОТЕКТИВНОГО ДЕЙСТВИЯ ИМБИРЯ *ZINGIBER OFFICINALE* ПРИ ИНТОКСИКАЦИИ АЛЮМИНИЕМ У КРЫС

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KEYWORDS: ginger extract, aluminium, oxidative stress, liver, kidney, brain.

КЛЮЧЕВЫЕ СЛОВА: экстракт имбиря, алюминий, окислительный стресс, печень, почки, головной мозг.

ABSTRACT. There is increasing interest in the study of the antioxidant properties of plant phenolic compounds as evidence shows that consumption of these compounds contributes to protection from a number of ailments including neurodegenerative disorders. Ginger (*Zingiber officinale*) is a folk medicine. The aim of the study is to demonstrate the protective effect of ginger extract against aluminium-induced toxicity in rat model. Animals received aluminium nitrate at a dose of 32.5 mg/kg (1/2 LD_{50} of $Al(NO_3)_3$ *i.p.*) once only for the induction of toxicity. Different doses of hydroalcoholic extract of ginger (25, 50 and 100 mg/kg) was administered for 3 days after 24 h of aluminium exposure. Significant rise in liver biochemical markers such as AST and ALT whereas serum protein was found to be declined after toxicant exposure. The activity of δ-aminolevulinic acid dehydratase in blood and δ-aminolevulinic acid synthetase in brain was decreased after aluminium exposure. Creatinine, urea, triglyceride level in serum, total and esterified cholesterol in tissues were increased. TBARS level was significantly higher and total glutathione content was significantly lowered during toxicity in liver, kidney and brain. Ginger extract attenuated oxidative stress by scavenging various free radicals produced by aluminium. It stimulated antioxidant enzymes and recovered all the biochemical variables towards control. Histopathological changes in liver, kidney and brain were also recouped with the therapy of ginger. In conclusion, hydroalcoholic ginger extract has potential to recoup aluminium induced dysfunction and oxidative damage.

РЕЗЮМЕ. В настоящее время наблюдается растущий интерес к изучению антиоксидантных свойств фенольных соединений растительного происхождения, поскольку показано, что употребление этих веществ способствует защите от ряда заболеваний, включая нейродегенеративные расстройства. Имбирь (*Zingiber officinale*) представляет собой средство народной медицины. Целью исследования является демонстрация защитного эффекта экстракта имбиря против интоксикации, вызванной алюминием у крыс. Животные получали нитрат алюминия в дозе 32,5 мг/кг (1/2 $ЛД_{50}$ $Al(NO_3)_3$ в/б) однократно для индукции интоксикации. Спустя сутки после инъекции животным в течение 3 дней вводили водно-спиртовой экстракт имбиря в различных дозах (25, 50 и 100 мг/кг). В течение интоксикации было обнаружено значимое увеличение в печени биохимических маркеров, таких как АСТ и АЛТ, при снижении сывороточного белка. Активность дегидратазы δ-аминолевулиновой кислоты в крови и синтетазы δ-аминолевулиновой кислоты в мозге снизилась. Уровень креатинина, мочевины, триглицеридов в сыворотке крови, общий и этерифицированный холесте-

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рин в тканях были увеличены. Уровень TBARS был значимо повышен, а общее содержание глутатиона значимо снижено в печени, почках и мозге. Экстракт имбиря ослаблял окислительный стресс за счет удаления свободных радикалов, образуемых алюминием. Это стимулировало антиоксидантные ферменты и приближало все биохимические параметры к наблюдаемым в контроле. Гистологические изменения в печени, почках и мозге также компенсировались при терапии имбирем. Таким образом, водно-спиртовой экстракт имбиря потенциально позволяет компенсировать дисфункции и окислительные повреждения, вызываемые алюминиевой интоксикацией.

INTRODUCTION

Aluminium (Al), an environmental xenobiotic is prevalent in daily life and interferes with several biological processes. Aluminium metal is abundantly present in the earth's crust, from the environment it gets access to the human body. It is a constituent of cooking utensils, medicines such as antacids, deodorants and food additives, also from corn, yellow cheese, salt, herbs, spices, tea, cosmetics, ware and containers (Newairy et al., 2009).

Al crosses the blood-brain barrier and forms deposits in brain regions such as the striatum, hippocampus and occipital cortex, recently, it has been demonstrated that, increased concentration of Al in brain has also been observed in neuritic deposits, plaques and neurofibrillar tangles in Alzheimer's Disease .It gains access to the brain via the specific high affinity receptors for transferrin (TfR) causes synaptic structural abnormalities thereby resulting in profound memory loss (Sharma et al., 2009).

Al contributes to numerous disorders and affects several enzymes and other biomolecules relevant to Alzheimer‘s disease, cause neurological symptoms, biochemical responses leading to unhealthy bone metabolism and learning disabilities in children (Lukiw et al., 1998). Al also accumulates in mammalian tissues such liver and kidney, this accumulation is accompanied by renal failure and promotes degeneration in renal tubular cells (Mahieu et al., 2009).

It would be of great interest to find out whether food supplements endowed with antioxidative potential could prevent/reverse or reduce the Al induced alterations. Epidemiological studies suggest that dietary intake of antioxidants from fruits and vegetables is associated with a reduced risk of ailments. Phenolic compounds are widely distributed in plants. Ginger rhizome (Gin, *Zingiber officinale* R., family Zingiberaceae) is commonly used as spice worldwide and an equally as Indian medicine and possesses biological activities like anticancer, anti-oxidation, antihistaminic, antihypercholesterolemic and antihyperlipidaemic (Shanmugam et al., 2010). An antioxidant activity is due to the presence of phenols, gingerol and zingerone (Masuda et al., 2004). It also contains biotrace elements, vitamin C and phenolic acids. Ginger's active principles protect nerve cells and may have potential in the treatment of Alzheimer's disease *in vitro* (Kim et al., 2005).

The present study was thus designed to evaluate the antioxidant potential of hydroalcoholic ginger extract against aluminium-induced toxicity in rat model.

MATERIALS AND METHODS

Experimental animals:

Thirty Sprague Dawley female albino rats weighing 160 ± 10 g from departmental animal facility were selected. They received a standard pellet diet (Pranav Agro Industries, New Delhi, India having metal contents in ppm dry weight Cu, 10; Mn, 33; Zn, 45; and Co, 5) and drinking water *ad libitum*. Animals used in this study were treated and cared for in accordance with the guidelines recommended by the Committee for the Purpose of Control and Supervision of Experiments on Animals, Government of India, Ministry of Culture, Chennai.

Chemicals:

Aluminium nitrate (Qualigens, India product no 21255) and other analytical grade laboratory reagents were procured from Merck (Germany), HiMedia and Glaxo Chemical (India).

Extract preparation:

Ginger was procured from local market. The slices of rhizome were dried in shade and powdered (250 g). Ginger powder mix with 50% alcohol (1 litre) and shaking everyday for 15 days. The extract was filtered and evaporated to finally obtain as brown semisolid. An aqueous suspension of crude extract was administered to the animals orally according to their body weight. Since Ginger is a water-soluble spice, hydrogen compounds activate water-soluble spices. The main active ingredient in ginger is components called gingerols which are soluble in alcohol, thus hydro alcoholic extract was prepared. Doses were selected on the basis of previous studies (Shanmugam et al., 2010).

Experimental design:

Group 1: Control (received vehicle only).

Group 2: Aluminium nitrate
(1/2 LD_{50} = 32.5 mg/Kg, *i.p.* once only)

Groups 3–5: Al (as group 2) + Ginger extract (25, 50 and 100 mg/Kg, *p.o.* for 3 days)

Animals of all the groups were sacrificed after 48 hours of last treatment for biochemical and histopathological analyses.

Evaluation of antioxidant properties:

Free radical scavenging activity was measured by 1, 1-diphenyl-2-picryl-hydrazyl (DPPH). The antioxidant activities of the ginger (100–500 µg/ml) and standard vitamin C (10–50 µg/ml) were assessed on the basis of the radical scavenging effect of the stable DPPH free radical (Blois, 1958). Vitamin C was used as the positive reference.

Quantitative estimation of total phenolic contents

The total phenolic content of ginger extract was determined with Folin–Ciocalteu reagent in alkaline me-

dium using tannic acid as standard (Slinkard, Singleton, 1977). The total phenolic content was expressed in µg of tannic acid equivalents/mg of extract.

Biochemical assays:

Blood was collected from retro-orbital venous sinus and serum was isolated for the estimation of aspartate aminotransferase (AST) and alanine transaminase (ALT) (Reitman, Frankel, 1957). The ketoacids present react with 2,4-dinitro phenyl hydrazine to give brown coloured hydrozones, which absorb maximally at λ 510 nm. Serum protein (Lowry et al., 1951), serum cholesterol, triglyceride, creatinine and urea were estimated by autoanalyser Microlab, 200 (Merck, Germany) using E-Merck kit methods. Activity of δ-aminolevulinic acid dehydratase (ALAD) (Berlin, Schaller, 1974) was determined in blood. The activity of acetylcholinesterase (AChE) was determined in fore, mid and hind brain (Ellman et al., 1961). Homogenate in an isotonic solution was processed for total and esterified cholesterol (Zlatkis et al., 1953).

Homogenates (10% w/v) were prepared in 0.15 M KCl for LPO whereas liver homogenate (5% w/v) was prepared in 1% sucrose solution for the estimation of GSH. Hepatic, renal and cerebral lipid peroxidation (LPO) was measured by estimation of thiobarbituric acid reactive substances (TBARS) as described by Sharma and Krishna Murti (Sharma, Krishnamurthy, 1968) and reduced glutathione (GSH) (Brehe, Bruch, 1976) was estimated using dithionitrobenzoic acid (DTNB). The activity of δ-aminolevulinic acid synthetase (ALAS) was also determination in brain (Maines, 1980).

Histopathological assays:

Liver, kidney and brain were dissected out washed in saline and fixed in Bouin's fluid, embedded in paraffin, sectioned at 6µm and stained with haemotoxylin and eosin for examination by light microscopy.

Statistical analysis:

P values at the level of ≤ 0.05 were evaluated by student's t test. Significance of the difference among various groups was evaluated by one way analysis of variance (ANOVA) F (Snedecor, Cochran, 1994).

RESULTS

Antioxidant activity of ginger extract:

DPPH assay is widely used as a free radical to evaluate the antioxidant activity of natural compounds. Graph 1 demonstrates the antioxidant activity of ginger extract using DPPH dye. Ginger extract at different doses, i.e. 10–50 g/ml showed free radical scavenging activity in dose dependent manner. Maximum percentage inhibition of DPPH radicals by the ginger extract was about 88% at 50 g/ml concentration. Standard drug ascorbic acid showed about 86% inhibition of the DPPH radicals at 50 g/ml. The amount of phenolic components was calculated as tannic acid equivalents. It was found to be 62.5 µg/mg in samples indicating considerable free radical scavenging activity.

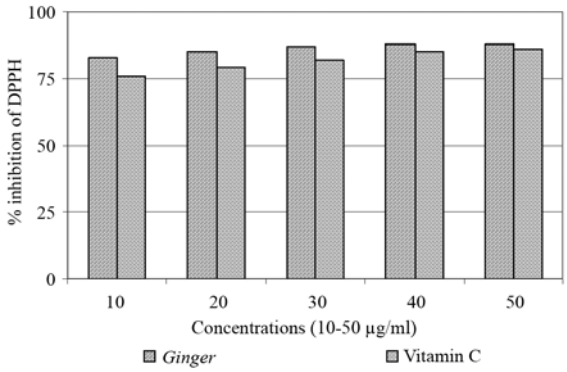


***Fig. 1**. Antioxidant activity of ginger extract*

Biochemical Changes:

Oral administration of extract of ginger caused neither any behavioural changes nor mortality up to 100 mg/(kg). Table 1 reveals that Al administration provoked significant rise in serum transaminases (AST & ALT) but reduced serum protein level. The activity of ALAD in blood was also inhibited after toxicant exposure. With the therapy of ginger extract at 50 and 100 mg/(kg) showed protective effect. The results presented in this investigation demonstrate significant (P ≤ 0.05) rise with regard to urea, creatinine, cholesterol and triglyceride after Al administration. Different doses of ginger extract restored all the variables towards control in a dose dependent manner (Table 2). The activity levels of AchE of different experimental groups along with the controls are shown in the Table 3. It is reduced in fore, mid and hind brain after Al exposure. The data was analysed statistically using one way of analysis of variance. Therapy with ginger extract showed significant improvement in this parameter. The activities of ALAS in brain recorded a decrease under toxicant exposure and the restored value was noted after receiving ginger extract for three days (Table 3). Al caused drastic decline in the hepatic, renal and cerebral GSH, whereas LPO was significantly increased in all the organs. With the treatment of ginger extract GSH and LPO was found towards normal (Table 4). Total and esterified cholesterol exhibited a significant (P ≤ 0.05) increase in Al exposed groups in liver, kidney and brain. Ginger extract co-treated groups showed control values (Table 5). Small amount of Al was found in liver, kidney and brain of rat. Al body burden was enhanced after Aluminium administration (P ≤ 0.05) in all the organs. The accumulation of Al was in the order liver > kidney > brain. Therapy of ginger extract was significantly reducing the body burden of Al (Table 6).

Histopathological changes:

Histopathology of liver from normal control group showed normal arrangement of hepatocytes with clearly brought out nuclei, central vein and portal triad (Fig. 1). Microscopical examination of Al treated liver section showed various degrees of pathological changes starting hypertrophy with hydropic changes, vacuolar degenerations and degeneration of hepatocytes (Fig. 2). Liver sections from groups treated by lower doses of ginger extract showed less

improvement (Fig. 3–4). Hepatocytes clearly showed plate like arrangements of the polyhedral hepatocytes, granulated cytoplasm with clear uniform nuclei Well-organized hepatic cords were separated by narrow blood sinusoids with the treatment of 100 mg/(kg) (Fig. 5). Histopathology of kidney from normal control group showed normal features (Fig. 6) Al caused degeneration in the areas of the renal cortex such as mesangial cellular proliferation, glomeruli filled the Bowman's capsule because of congestion and proximal tubular necrosis with desquamated necrotic epithelial cells in the lumen (Fig. 7). Lower doses of extract showed less improvement (Fig. 8, 9).The features include less degenerative changes with prominent glomeruli and tubular epithelium with the treatment of ginger extract (Fig. 10).Section of control rat brain showed the typical layered appearance of the cerebral cortex with clear Purkinje cells (Fig. 11). Al caused gross disorganization such as degeneration of large and small pyramidal cells, pyknosis, vacuolations and cavitations. Shrunken cells surrounded by edematous spaces were also observed in the molecular layer. The Purkinje cells had become irregular in shape with fragmentation of the nuclear mass (Fig. 12). Treatment with the ginger extract at 25 mg/kg dose depicted not much improvement; however improvement in Purkinje cells of cerebrum were clear at 50 and 100 mg/kg dose of rats and (Fig. 13–15).

Table 1. ***Influence of ginger extract in the activities of serum AST, ALT, protein and blood ALAD against aluminium in rats***

Treatments	ALAD (nmol/min/ ml erytrhocytes)	AST (IU /L)	ALT (IU /L)	Serum Protein (mg /100 ml)
Control	7.75 ± 0.42	67.2 ± 3.71	41.1 ± 2.27	40.1 ± 2.21
Al	3.18 ± 0.17$^{\#}$	155 ± 8.56$^{\#}$	125 ± 6.91$^{\#}$	24.9 ±1.37$^{\#}$
Al + G_{25}	5.99 ± 0.33*	113 ± 6.27*	68.5 ± 3.78*	37.2 ± 2.05*
Al + G_{50}	6.85 ± 0.37*	110 ± 6.08*	63.5 ± 3.51*	38.1 ± 2.10*
Al + G_{100}	7.15 ± 0.39*	103 ± 5.69*	62.0 ± 3.42*	39.1 ± 2.16*
ANOVA (F value)	31.0$^{@}$	29.9$^{@}$	64.8$^{@}$	11.6$^{@}$

Values are mean ± SEM; N = 6; # P ≤ 0.05 vs control group; * P ≤ 0.05 vs Al administered group; ANOVA (F values)$^{@}$ = = Significant at 5 % level.

Table 2. ***Influence of ginger extract in the activities of serum urea, creatinine, triglycerides and cholesterol against aluminium in rats***

Treatments	Urea (mg/dl)	Creatinine (mg/dl)	Triglycerides (mg/dl)	Cholesterol (mg /dl)
Control	19.7 ± 1.08	0.19 ± 0.01	68.6 ± 3.79	46.4 ± 2.56
Al	55.3 ± 3.05$^{\#}$	0.83 ± 0.04$^{\#}$	94.1 ± 5.20$^{\#}$	74.6 ± 4.12$^{\#}$
Al + G_{25}	45.0 ± 2.48*	0.45 ± 0.02*	80.0 ± 4.42*	54.1 ± 2.99*
Al + G_{50}	41.0 ± 2.26*	0.45 ± 0.02*	72.7 ± 4.01*	50.5 ± 2.79*
Al + G_{100}	37.0 ± 2.04*	0.43 ± 0.02*	71.3 ± 3.94*	47.8 ± 2.64*
ANOVA (F value)	39.2$^{@}$	75.2$^{@}$	6.84$^{@}$	16.8$^{@}$

Values are mean ± SEM; N = 6; # P ≤ 0.05 vs control group; * P ≤ 0.05 vs Al administered group; ANOVA (F values)$^{@}$ = = Significant at 5 % level.

Table 3: ***Influence of ginger extract in the activities of AchE and ALAS in brain against aluminium in rats***

Treatments	Acetyl cholinesterase (μmole / min / mg protein)		ALAS (nmol/min/ mg Protein)	
	Fore Brain	Mid Brain	Hind Brain	Brain
Control	40.9 ± 2.26	21.2 ± 1.71	40.2 ±2.22	11.7 ± 0.64
Al	17.7 ± 0.97$^{\#}$	9.44 ± 0.52$^{\#}$	21.1 ±1.16$^{\#}$	3.99 ± 0.22$^{\#}$
Al + G_{25}	25.5 ± 1.40*	12.3 ± 0.67*	26.2 ±1.44*	7.99 ± 0.44*
Al + G_{50}	28.7 ± 1.58*	12.6 ± 0.69*	28.9 ±1.59*	7.98 ± 0.44*
Al + G_{100}	30.0 ± 1.65*	14.7 ± 0.81*	30.5 ±1.68*	8.20 ± 0.45*
ANOVA (F value)	31.7$^{@}$	35.9$^{@}$	21.4$^{@}$	42.1$^{@}$

Values are mean ± SEM; N = 6; # P ≤ 0.05 vs control group; * P ≤ 0.05 vs Al administered group; ANOVA (F values)$^{@}$ = = Significant at 5 % level.

Table 4. ***Influence of ginger extract on TBARS and glutathione level in liver, kidney and brain against aluminium in rats***

Treatments	Lipid peroxidation (nmole TBARS / mg protein)			Glutathione (µ mole / g)		
	Liver	Kidney	Brain	Liver	Kidney	Brain
Control	0.37 ± 0.02	0.68 ± 0.03	0.95 ± 0.05	7.20 ± 0.39	7.05 ± 0.38	7.07 ± 0.39
Al	1.31 ± 0.72$^{\#}$	1.91 ± 0.10$^{\#}$	2.14 ± 0.12$^{\#}$	5.05 ± 0.27$^{\#}$	3.34 ± 0.18$^{\#}$	3.71 ± 0.20$^{\#}$
Al + G_{25}	0.47 ± 0.02*	1.23 ± 0.06*	1.49 ± 0.08*	6.15 ± 0.33*	6.20 ± 0.34*	6.59 ± 0.36*
Al + G_{50}	0.46 ± 0.02*	1.20 ± 0.06*	1.16 ± 0.06*	6.17 ± 0.34*	6.27 ± 0.34*	6.60 ± 0.36*
Al + G_{100}	0.45 ± 0.02*	1.20 ± 0.06*	1.05 ± 0.05*	6.32 ± 0.34*	6.67 ± 0.36*	6.90 ± 0.38*
ANOVA (F value)	121$^{@}$	44.2$^{@}$	44.9$^{@}$	5.94$^{@}$	23.3$^{@}$	19.2$^{@}$

Values are mean ± SEM; N = 6; # P ≤ 0.05 vs control group; * P ≤ 0.05 vs Al administered group; ANOVA (F values)$^{@}$ = = Significant at 5 % level.

Table 5. ***Influence of ginger extract on cholesterol in liver, kidney and brain against aluminium in rats***

Treatments	Total Cholesterol (mg /100 mg)			Esterified Cholesterol (mg /100 mg)		
	Liver	Kidney	Brain	Liver	Kidney	Brain
Control	0.12 ± 0.006	0.11 ± 0.006	0.10 ± 0.005	0.06 ± 0.003	0.04 ± 0.002	0.16 ± 0.009
Al	1.20 ± 0.066$^{\#}$	0.72 ± 0.039$^{\#}$	2.92 ± 0.161$^{\#}$	0.20 ± 0.011$^{\#}$	0.15 ± 0.008$^{\#}$	0.65±0.035$^{\#}$
Al + G_{25}	0.77 ± 0.042*	0.53 ± 0.029*	2.00 ± 0.110*	0.14 ± 0.008*	0.12 ± 0.006*	0.51 ± 0.028*
Al + G_{50}	0.69 ± 0.038*	0.45 ± 0.024*	1.90 ± 0.105*	0.12 ± 0.007*	0.11 ± 0.006*	0.44 ± 0.024*
Al + G_{100}	0.54 ± 0.030*	0.37 ± 0.020*	1.60 ± 0.088*	0.11 ± 0.006*	0.10 ± 0.005*	0.42 ± 0.023*
ANOVA (F value)	105$^{@}$	84.6$^{@}$	109$^{@}$	50.6$^{@}$	54.1$^{@}$	57.1$^{@}$

Values are mean ± SEM; N = 6; # P ≤ 0.05 vs control group; * P ≤ 0.05 vs Al administered group; ANOVA (F values)$^{@}$ = = Significant at 5 % level.

Table 6. ***Influence of ginger extract on metal concentration (µg/g) in liver, kidney and brain against aluminium in rats***

Treatments	Liver	Kidney	Brain
Control	16.70 ± 0.92	16.50 ± 0.89	13.50 ± 0.71
Al	34.60 ± 1.91$^{\#}$	44.00 ± 2.43$^{\#}$	44.00 ± 2.43$^{\#}$
Al + G_{25}	17.35 ± 0.95*	19.16 ± 1.05*	15.98 ± 0.88*
Al + G_{50}	15.16 ± 0.83*	15.16 ± 0.83*	13.90 ± 0.76*
Al + G_{100}	11.87 ± 0.65*	13.96 ± 0.77*	13.73 ± 0.75*
ANOVA (F value)	72.4$^{@}$	104$^{@}$	127$^{@}$

Values are mean ± SEM; N = 6; # P ≤ 0.05 vs control group; * P ≤ 0.05 vs Al administered group; ANOVA (F values)$^{@}$ = = Significant at 5 % level.

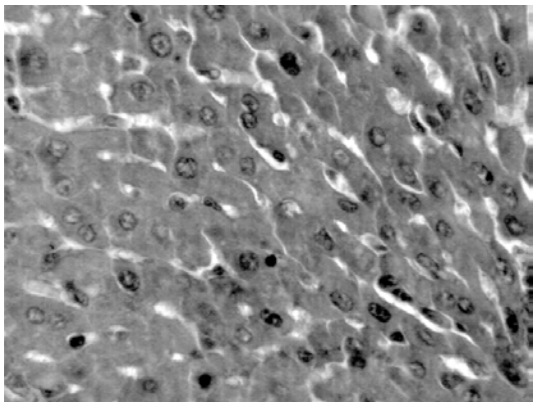


Fig. 1. *Control rat liver showing essentially normal liver architecture. H and E ×400*

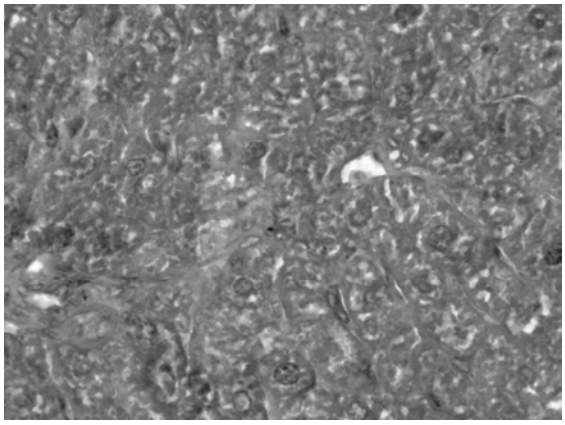


***Fig. 2**. Liver exposed to Al, note hydropic degeneration in the centrilobular area. H and E ×400*

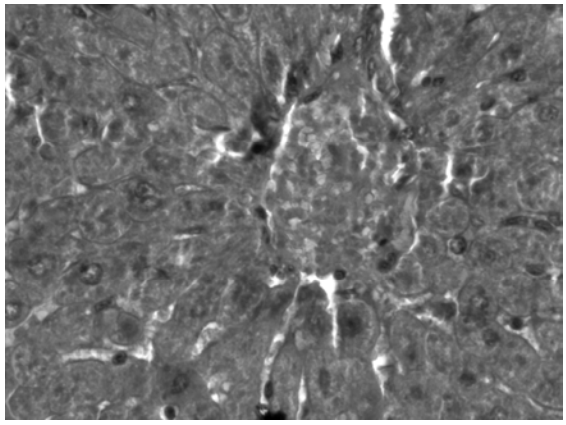


***Fig. 3.** Liver of rat treated with 25 and 50 mg/kg extract, note degenerated nuclei, hepatocytes showing vacuolation. H and E ×400*

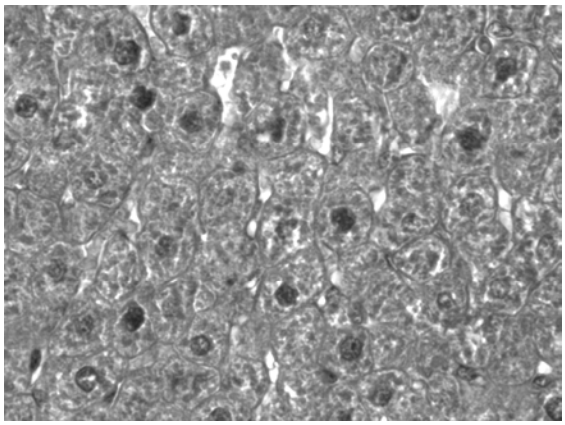


***Fig. 4.** Liver of rat treated with 25 and 50 mg/kg extract, note degenerated nuclei, hepatocytes showing vacuolation. H and E ×400*

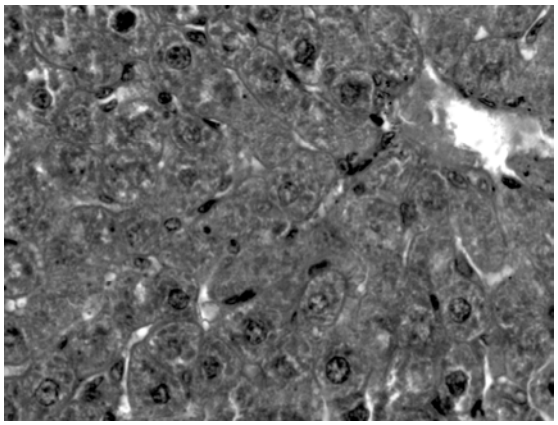


***Fig. 5.** Liver of rat treated with 100 mg/kg ginger extract showing normal architecture with normal hepatocytes, sinusoids as well as well formed nuclei. H and E ×400*

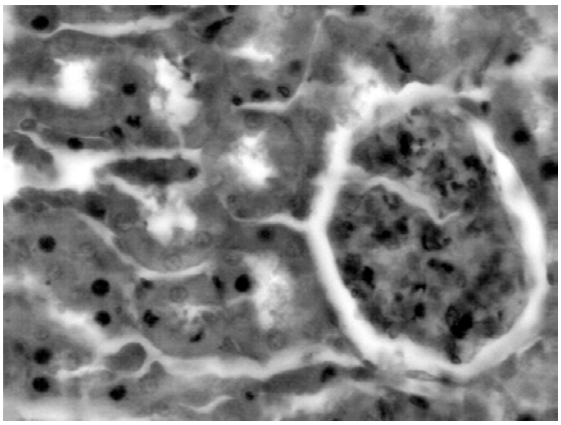


***Fig. 6.** Control rat kidney showing essentially normal features. H and E ×400*

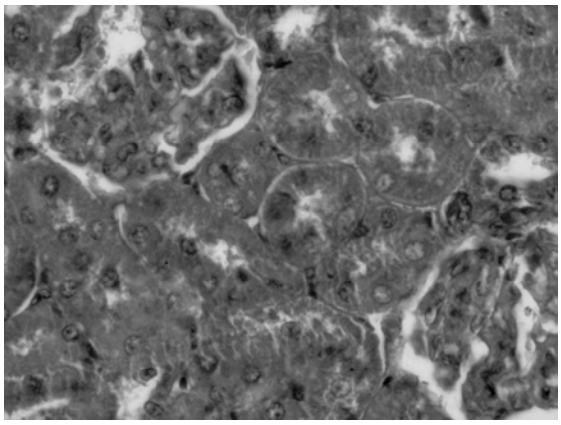
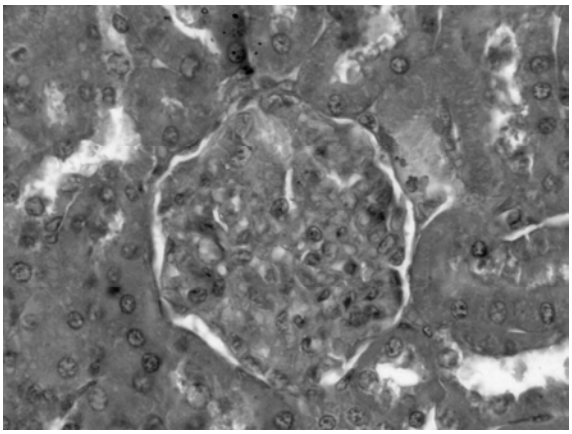


***Fig. 7.** Kidney exposed to Al showing degeneration of the glomeruli, tubular degeneration in the cortical as well as in the medullary area. H and E ×400*



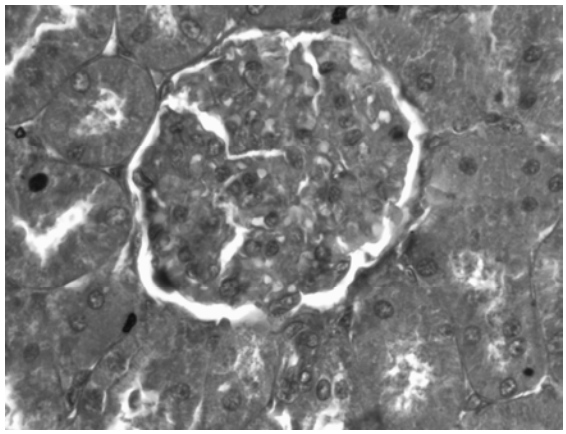


Fig. 8–9. *Treatment of ginger extract at 25 and 50 mg/kg showing less improved tubules and glomeruli. H and E ×400*

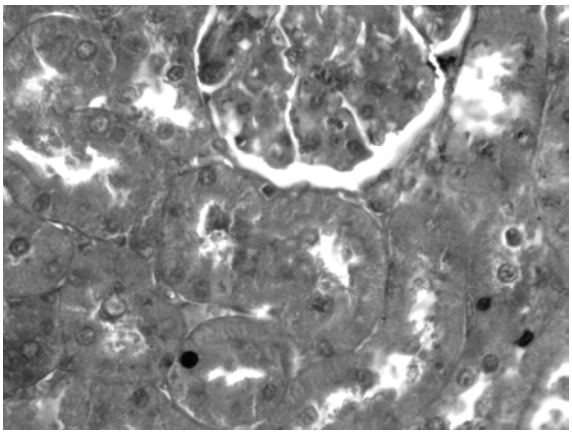


Fig. 10. *Treatment of ginger extract at 100 mg/kg showing the normal architecture of tubules and glomeruli. H and E ×400*

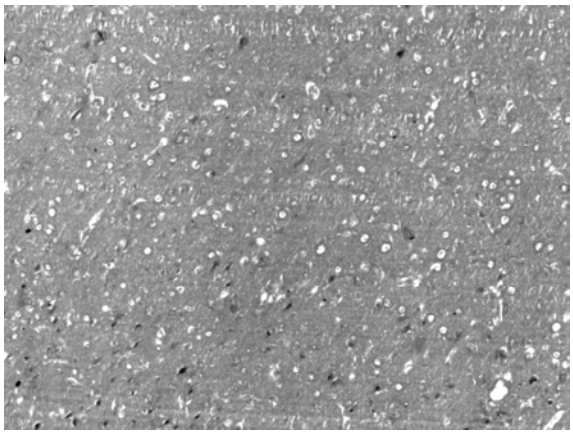


Fig. 11. *Control rat brain showing essentially normal features. H and E ×100*

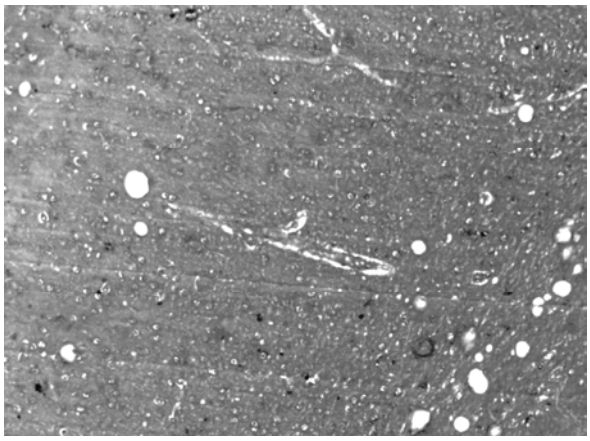


Fig. 12. *Al exposed section showing disorganization of the typical layered appearance of the cerebral cortex with neurodegeneration, pyknosis and vacuolations. H and E ×100*

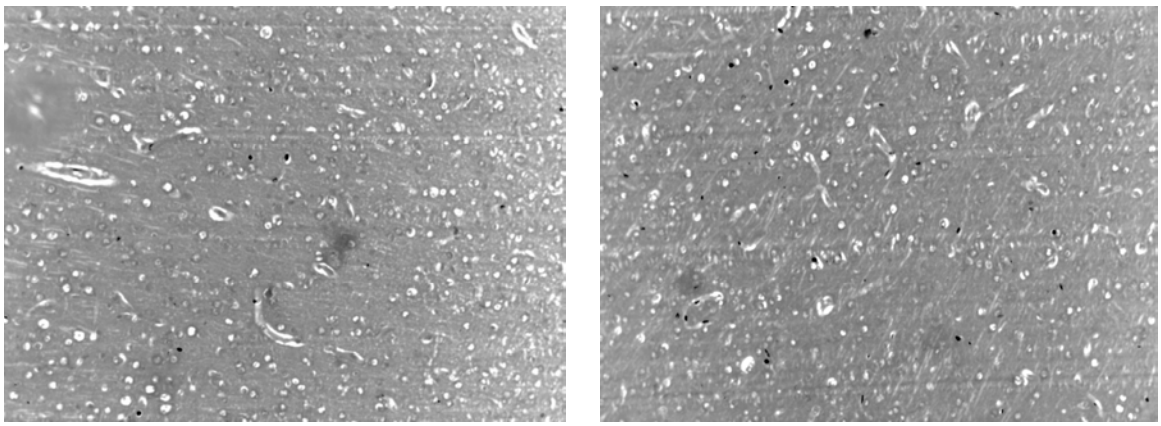


Fig. 13–14. *Treatment with 25 and 50 mg/kg ginger extract showing comparatively less improvement (Compare fig 15). H and E ×100*

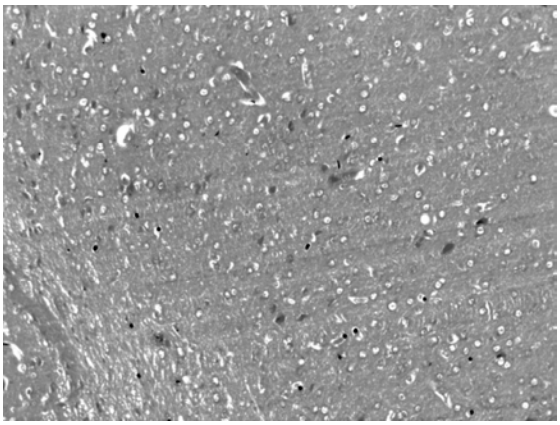


Fig. 15. *Treatment with 100 mg/kg ginger extract against Al showing well formed layers with distinct nuclei. H and E ×100*

DISCUSSION

The present study was carried out to investigate the protective effects of ginger extract on Al induced oxidative stress and biochemical alterations in rats. Al has a strong prooxidant activity in spite of its non-redox status (Exley, 2004). Its toxicity may be mediated by free radical generation and alterations in antioxidant enzymes *in vivo* and *in vitro* (Tabaldi et al., 2009), which caused neurotoxicity (Tabaldi et al., 2009), nephrotoxicity (Mahieu et al., 2009) and hepatotoxicity (Rodella et al., 2008).

Results reveal that Al provoked significant alterations in the activities of serum AST and ALT, its accumulation in the liver and can be toxic to the hepatic tissue changes in these enzymatic activities may be due to the leakage of these enzymes from the liver cytosol into the blood stream resulting in the pathology involving necrosis of the liver and kidney, this is in agreement with previous studies (Mohamed, Awad, 2008; Shati, Alamri, 2010; Turkez et al., 2010). AST significantly increases in such cases and escapes to the plasma from the injured hepatic cells. In addition, ALT level is of value also indicating the existence of liver diseases, as this enzyme is present in large quantities in the liver. It increases in serum when cellular degeneration or destruction occurs.

The present results revealed that Al decreased serum protein. The inhibitory effect of Al on protein profile is in agreement with the finding of Yousef (2004). The elevation in serum urea and creatinine levels in Al treated rats is considered as a significant marker of renal dysfunction or may be related to metabolic disturbances (e.g. renal function, cation–anion balance) and this is supported by the finding of various authors (Mohamed, Awad, 2008; Shati, Alamri, 2010; Turkez et al., 2010). The increase in urea concentrations in serum of animals treated with Al may be due to its effect on liver function, as urea is the end-product of protein catabolism and this is confirmed by the decrease in serum proteins and/or referred to liver dysfunction as proven by the increase in plasma AST and ALT activities. Serum urea and creatinine levels were restored by ginger extract in alcohol, acetaminophane and doxorubicin treated groups (Yemitan, Izegbu, 2006; Ajith et al., 2007; Shanmugam et al., 2010). The increase in serum triglycerides is possibly due to hypoactivity of lipo-

protein lipase in blood vessels which breaks up triglycerides. High serum cholesterol level may be due to hepatic dysfunction by Al (Pandya et al., 2004; Yousef, 2004; Ajith et al., 2007; Mohamed, Awad, 2008; Shati, Alamri, 2010; Turkez et al., 2010). Ginger extract decreased hepatic triglyceride, cholesterol levels in the study. These finding are also noted by various authors in the rats fed with high-fat diet (Ajith et al., 2007; ICMR, 2003).

The ionic radii of Al^{3+} most closely resembles those of Fe^{3+}, therefore it binds to Fe^{3+} carrying protein transferrin, thus reduces the binding of Fe^{2+}. This increase in free intracellular Fe^{2+} causes the peroxidation of membrane lipids and thus membrane damage (Nehru, Anand, 2005). In the present experiment Al administration enhanced the LPO in liver, kidney and brain but caused a significant decline in the GSH level. Elevation of LPO was evident by the increased production of TBARS, which suggests participation of free-radical induced oxidative cell injury. These observations are similar to the data reported by previous studies (Yousef, 2004; Newairy et al., 2009). Therapy of ginger at 50 and 100 mg/kg doses provoked considerable recovery. GSH plays an important role in the detoxification and metabolism of many xenobiotic compounds. The decrease in SH group of GSH content was found in the various studies (Yousef, 2004; Newairy et al., 2009). These effects may reflect the ability of extract to enhance the scavenging and inactivation of H_2O_2 and hydroxyl radicals (ICMR, 2003). A significant decrease in the AChE of fore, mid and hind brain after Al exposure indicates interference with either synthesis of AChE or inhibit choline uptake by synaptosomes. Al also binds with the active site of AChE hence, decreases the activity. When this enzyme is inhibited Ach is not hydrolyzed and accumulates in cholinergic sites causing alteration in the normal nervous system function and thus significant decrease in the acetylcholine esterase activity (Lukiw et al., 1998; Nehru, Anand, 2005; Newairy et al., 2009). The antioxidant compounds, like gingerol, shogals, ketone compounds and phenolic compounds of ginger were responsible for scavenging the superoxide anion radicals (Cao et al., 1993; ICMR, 2003).

Activity of ALAD in blood and ALAS in brain was significantly decreased after Al exposure. These are first and second rate-limiting enzymes of heme biosynthesis which is localized in mitochondria. The reduced level of hemoglobin can be associated with hemolysis or disturbances in heme biosynthesis. In order to inhibit ALAD, aluminium might be crossing the erythrocyte membrane. In microscopic study, Al treated liver section showed hypertrophy with hydropic changes, sinusoidal dilatation, degeneration of hepatocytes in liver (Turkez et al., 2010) and in the areas of the renal cortex and medulla. Disorganization in the layers of cerebrum and vacuolar spaces were also observed following Al exposure. Thus, ginger may exert a beneficial effect in countering the toxic free radicals in liver, kidney and brain. Ginger and its combination with vitamin E protect the kidney in cisplatin and in brain monosodium glutamate trated group (Cao et al., 1993; ICMR, 2003).

In summary the present biochemical data confirm that hydroalcoholic extract of ginger may protect against acute Al induced oxidative stress via its antioxidant and free radical-scavenging properties. Our findings provide biochemical evidence for the efficacy of extract in attenuating the adverse effects in the brain, liver and kidney of rats. Ginger feeding confers protection because of the presence of free phenolic and hydrolysed phenolic fractions which may scavenge the superoxide anion radicals or it enhance the status of defence enzymes. Antioxidant bioactive compounds like as gingerols, shogals, ketones (Cao et al., 1993; ICMR, 2003) are also responsible for enhancing the activity of phase II detoxification enzymes (ICMR, 2003). Moreover, ginger is a natural polyphenolic compound that is already used clinically and is approved by the Food and Drug Administration as a safe food additive. The results confirm the popular use of ginger for its medicinal properties in Ayurveda and folklore medicines. These results further suggest the use of ginger for disorders that needs to be considered as possibilities for new therapeutic approaches.

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