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International Journal of Current Research
Vol. 10, Issue, 03, pp.67381-67387, March, 2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

CINNAMON ZEYLANICUM ATTENUATES OXIDATIVE STRESS AND IMPROVES NEUROBEHAVIORAL ACTIVITY IN LEAD INDUCED NEUROTOXICITY

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ARTICLE INFO

Article History:
Received 27th December, 2017
Received in revised form
05th January, 2018
Accepted 20th February, 2018
Published online 30th March, 2018

Key words:
Lead, Neurotoxicity,
Behavioral, Biochemical,
Cinnamon oil and Rats.

ABSTRACT

The present study has been carried out to investigate the neuroprotective activity of cinnamon (*Cinnamon zeylanicumin)* on lead induced neurotoxicity and behavioral impairments in rats. Different behavioral parameters and biochemical assays in brain of rats were observed. Rats exposed to lead (lead acetate 5.0mg/kg body weight p.o. for 28 days) caused a significant decrease in body weight, brain weight and behavioral changes as compared to controls. The increased levels of lead in blood and brain also increases the levels of ROS, LPO and decreases the levels of GSH with concomitant reduction in SOD, CAT and GPx activities in brain of rats treated with lead as compared to controls. Co-treatment of lead with cinnamon oil (75mg/kg body weight p.o. for 28 days) decreases the levels of ROS, LPO and increases the level of GSH, SOD, CAT and GPx activity and showed improvements in behavioral changes as compared to lead treated groups. The results obtained were compared with vitamin E (100 mg/kg body weight p.o. for 28 days)as the standard antioxidant drug. Our results suggested that, cinnamon oil causes improvement in behavioral deficits and oxidative stress similar to that of standard drug, vitamin-E. This work reveals the potential of cinnamon oil as a protective drug for lead induced neurotoxicity and associated human health risk.

Citation: Akash Rawat, Sneha Yadav, Sandeep Kumar, Rajendra Nath, Prabha Verma and Pramod Kumar Singh, 2018. "*Cinnamon zeylanicum* attenuates oxidative stress and improves neurobehavioral activity in lead induced neurotoxicity", *International Journal of Current Research*, 10, (03), 67381-67387.

INTRODUCTION

Lead is ubiquitous non-essential toxic heavy metal found in the environment with potential danger to humans, animals and plants. Lead exposure are mostly occurs through petroleum products, leaded paints and drinking water, which is connected with the hepatic, renal, cardiovascular, bone, immune and brain disorders (Whit *et al*., 2007; Spivey, 2007; Murata *et al*., 2009). Particularly, the developing nervous system is more vulnerable to the toxicity of lead; therefore children are at a higher risk to its toxicity (Lidsky and Schneider, 2006). Occupational and industrial exposure to lead among workers results in accumulation of lead in their body organs and tissues (Menke *et al*., 2006). Epidemiological studies have reported that chronic lead exposure may cause CNS injury in children and also affects their growth, hearing ,short-term memory, intelligence and even brain damage and death (Cleveland *et al*., 2008).

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Studies have also shown that exposure to lead induced a broad range of physiological, biochemical, apoptotic and behavioral dysfunctions in animals and humans (Flora *et al*., 2008).Peripheral neuropathy have also been detected in lead neurotoxicity that further causes decreased motor activity due to loss of myelin sheath and thus impaired the signal transmission between nerves, muscular weakness, especially of the exterior muscles, lack of muscular coordination and fatigue (Sanders *et al*., 2009). Medicinal plants, natural antioxidants and metal chelating agents have been used to investigate their protection against heavy metal toxicity (El-Nekeety *et al*., 2009; Hossain *et al*., 2016; Singh *et al*., 2016). The aggregate evidences supported the beneficial effect of cinnamon oil in a variety of neurological and neurodegenerative conditions, but with variable results (Peterson *et al*., 2009). Cinnamon (*Cinnamomum zeylanicum*), is a medicinal plant belongs to Luaraceae family. The constituents of cinnamon are cinnamaldehyde, cinnamic acid and cinnamate, which are present in the essential oil thus contributing to the various biological activities (Yeh *et al*.,

2013). It is rich in natural polyphenolic compound. Polyphenols act as reactive oxygen and nitrogen species scavengers, redox-active transition metal chelators and enzyme modulators (Rice-Evans *et al*., 1997). Many studieshave been reported that cinnamon oil has antioxidant, anti-inflammatory, cardiovascular, antitumor, antimicrobial, antibacterial, immuno modulatory and cholesterol-lowering effects (Charles Denys, 2012; Rao and Gan, 2014). In view of continuation to the previous studies, the present study has been carried out to investigate the metal chelating properties and neuroprotective efficacy of cinnamon oil in lead induced changes in behavioral and biochemical parameters in brain of rats.

MATERIALS AND METHODS

Drugs and Chemicals

Cinnamon oil was purchased from Kama Ayurveda pharmacy, Mumbai (INDIA) and Vitamin-E was purchased from Merck Pharmaceuticals Ltd, Goa (INDIA).Lead acetate $(C_2H_3O_2)_2$ $Pb{\cdot}3H_2O$), Sodium chloride (NaCl), Potassium chloride (KCl),Disodium hydrogen phosphate (Na_2HPO_4), Potassium ortho phosphate (H_2KO_4P), Hydrochloric acid (HCl), Nitric acid (HNO_3), 2,7 dichlorodihydrofluorescein-diacetate (DCFH-DA), Ethylenediaminetetraacetate (EDTA), Hydrogen peroxide (H_2O_2), Perchloric acid ($HClO_4$), Nicotinamide adenine dinucleotide (NADH), 5,5-dithiobis 2-nitrobenzoic acid (DTNB), Trichloro acetic acid (TCA), Reduced glutathione (GSH) were purchased from Sigma-Aldrich, USA).

Animals and treatment

In our study, we used adult male rats (weight 180±20 g) of wistar strain (n=24) that were purchased from animal house of the Indian Institute of Toxicology Research (IITR), Lucknow, (UP) India. The animals were separately housed in polypropylene cages at room temperature (22 ± 2^0C) and relative humidity of 50±10 % and 12h light dark cycles. They have given free access to pellet diet and water ad libitum. All experiments were approved by the Institutional Animal Ethics Committee (wide letter no-80/IAH/Pharma-13) for the use of laboratory animals in accordance with the guidelines by the committee for the purpose of control and supervision of experiments on animals (CPCSEA), Ministry of Environment and Forests (Government of India), New Delhi, India.

The animals weredivided in to four groupswith six animals per group as follows

- Group I: treated with vehicle (distilled water**)** and served as control for 28 days.
- GroupII: treated with lead acetate (5.0 mg/kg b.wt./ oral; dissolved in distilled water) for 28 days.
- Group III: treated with lead acetate (5.0 mg/kg b.wt./oral) and *Cinnamon zeylanicumin* (75 mg/kg b.wt./oral; dissolved in 2% tween-20) for 28 days.
- Group IV: treated with lead acetate (5.0 mg/kg b.wt./ oral) and Vitamin-E (100 mg/kg b.wt./oral; dissolved in 2% tween-20, served as standard drug) for 28 days.

Neurobehavioral activities were carried out as per plan after the last dose of treatment. A set of five rats randomly selected from each treatment group were used to assess spontaneous locomotor activity, rota- rod performance. The same set of rats wasused to measure elevated plus maze test after 2h interval.

Neurobehavioral parameters

Spontaneous locomotor activity

Spontaneous locomotor activity in rats was investigated with the help ofActo-photometer. The movement of animals across the grills of the equipment was recorded as mentioned by (Ali *et al*., 1990). Effect of lead and the protective effect of cinnamon oil on total distance travelled were studied in rats of control and treated groups.

Rota - rod performance

The performance index of rats on equipment was monitored by standard procedure by (Rogers *et al*., 1997). Protective effect of cinnamon oil and toxic effect of lead on motor coordination was studied in rats using Rotomex-rota-rod equipment (Columbus Instruments, USA) and the time of fall was monitored from the rotating rod.

Elevated plus-maze test

Effect of lead exposure and the protective effect of cinnamon oilon time spent in open arms were recorded in control and treated rats by using elevated plus maze according to the method of Broad Hurst, 1960.

Blood collection and tissue homogenate preparation

After the neurobehavioral studies, rats were fasted for 12hrs before being anesthetized by injection (i.p.) of sodium pentothal (50 mg/kg b.wt.) solution. Blood sample was withdrawn through retro-orbital plexus and collected in EDTA-coated glass tubes for estimation of blood lead levels. There after five rats from each treatment group were sacrificed by cervical decapitation and immediately brains were excised, cleaned, weighed according to the method of Glowinski and Iversen, 1996. The whole brain was processed for the analysis of biochemical assays. The brain tissue (10% w/v) was homogenized in a phosphate buffered solution and centrifuged at 12000rpm for 15 min at 4^0 C. The supernatants were mixed with reaction mixture for analysis of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activity, reduced glutathione (GSH) and lipid peroxide (LPO) level. Rest of the brain tissue was homogenized in 10 μM DCFH-DA (2, 7-Dichloro Dihydrofluorescein Diacetate) for measurement of reactive oxygen species (ROS).

Biochemical parameters

Measurement of reactive oxygen species

ROS level in brain tissue was performed by the method of (Socci *et al*., 1999) by using 2, 7-dichlorodihydrofluorescin-diacetate dye that is converted into highly fluorescent 2, 7-dichlorofluorescin by cellular peroxides (including hydrogen peroxidation). Fluorescence technique was used to showed absorbance at 488-nm excitation and 525-nm emission wavelengths using a fluorescence plate reader. The amount of ROS level was expressed as nmol/min/mg protein in brain.

Assay of lipid peroxide

The level of LPO in brain tissue was estimated by the standard method of Ohkawa*et al*., 1997with few modifications and the intensity of pink color formed during the reaction was read at 532 nm. The amount of lipid peroxidation formed was expressed as n moles/mg of protein.

Assay of reduced glutathione

Reduced glutathione was assayed following the method of Ellman *et al*., 1950 with few modifications.GSH levels in brain were deprotonized by adding 1.5 ml TCA, an appropriate standard of GSH (1-10 µ moles) was also run simultaneously. The data was expressed as µ moles GSH /g tissue in brain.

Assay of superoxide dismutase activity

The activity of SOD in brain tissue was measured by the method of McCord and Fridovich, 1969, using NADH as a substrate in the post mitochondrial fraction of brain. The data was expressed as units/min/mg protein.

Assay of catalase activity

Catalase activitywas assayed according to method of Aebi, 1984, spectrophotometrically in post mitochondrial fraction using hydrogen peroxide (H_2O_2) as substrate with few modifications. The data was expressed as unit/min/mg protein.

Assay of glutathione peroxidase activity

Glutathione peroxidase activity was measured by the procedure of Pagila and Valentine, 1967, using few changes. The data was expressed as µg /min/mg protein.

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Protein estimation

Protein content was assayed by method of Lowry *et al*.,1951, using bovine serum albumin as a reference standard.

Lead Level

Estimation of lead levels in blood and brain

Lead levels in whole blood and brain were assessed as described by the method of Gupta and Gill, 2000. The absorbance was read by using graphite furnace atomic absorption spectrophotometer (GFASS) at 283 nm wavelength. A calibration curve was raised by adding known amounts of lead standard to calculate lead levels in the blood and brain tissue and data was expressed as µg/dl blood or µg/g wet tissue.

Statistical analysis

The data was expressed as the Mean ± S.E. The statistical analysis was carried out by Graph Pad Prism 5.0 using one way analysis of variance (ANOVA) followed by Newman-Keuls test for multiple pair wise comparisons among the groups. Values up to $P < 0.05$ have been considered significant.

RESULTS

Changes in body and brain weight

Effect of oral administration of lead (5.0 mg/kg b.wt.) in rats caused significant decrease in body weight (19%) in comparison to that of control. Co-treatment with lead and cinnamon oil (75mg/kg b.wt.) has shown improvement in body weight (11.4%) of rats as compared to that of lead intoxicated groups. Similarly, lead and vitamin-E exposed groups caused a significant increase in body weight (13.2%) as compared to those treated with lead alone groups. There was no significant change in brain weight between the groups(Table 1)

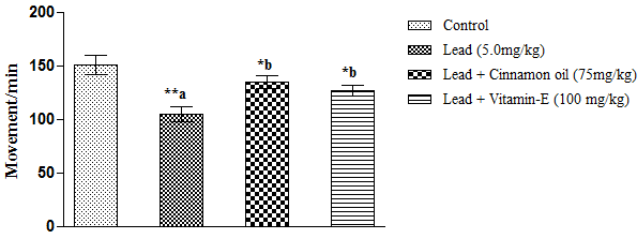
Table 1. Effect of lead, lead + cinnamon oil and lead + vitamin-E on body and brain weight of rats for 28 days

Group	Body Weight (g)	Brain Weight (g)
Control	337 ± 8.15	1.79 ± 0.07
Lead (5.0 mg/kg)	273 ± 6.81^{a,*}	1.66 ± 0.08^{ns}
Lead + cinnamon oil (5.0 +75mg/kg)	304 ± 11.00^{b,*}	1.72± 0.06^{ns}
Lead + vitamin-E (5.0 + 100mg/kg)	309 ± 11.77^{b,*}	1.75 ± 0.07 ^{ns}

All values are mean ± S.E. (n=5). a**(P < 0.01)-compared to control group,b* (P < 0.05)-compared to lead treated groups, ns-non significant

Effect on spontaneous locomotor activity

Toxic effect of lead in rats caused significant decrease in total distance travelled (30.5%), producing memory and cognition deficit as compared to rats in the control group. Whereas total distance travelled (28.6%) was increased in the co-treatment group as compared with lead treated alone group, also lead and vitamin-E intoxicated rats showed increased distance travelled (21.0 %), these parameters are briefed in Figure 1.

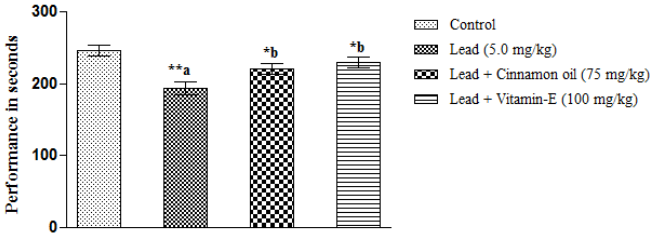


Values are mean ± S.E. (n=5).a**(P < 0.01)-compared to control group,b* (P < 0.05)-compared to lead treated groups.

Figure 1. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-E onSpontaneous locomotor activity of rats for 28 days

Effect on rota-rod performance

A significant impairment in motor coordination (21.1%) was observed in rats treated with lead as these rats fell rapidly from the rotating rod compared to that of control. It was noted that the rats simultaneously co-treated with lead and cinnamon oil stayed on the rotating rod for a longer period of time (13.9%) as compared to those treated with lead. Likewise, co-treatment with lead and vitamin-E caused longer period of time (18.6%) stayed on rotating rod (Figure 2).

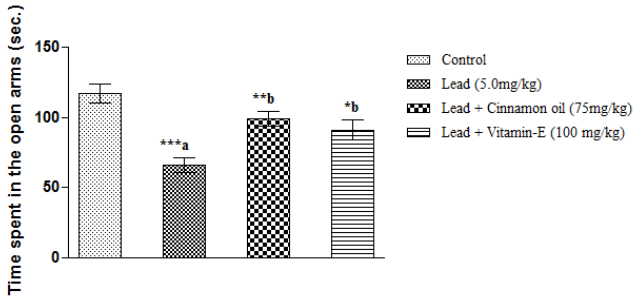


Values are mean ± S.E. (n=5). a**(P < 0.01)-compared to control group,b*(P < 0.05)-compared to lead treated groups

Figure 2. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-E onRota-rod performance of rats for 28 days

Effect on exploratory behaviour and anxietyusing elevated plus maze

Exposure to lead in rats have caused significantly less time spent in open arms (43.6%) and produced exploratory behavior and anxiety as compared to control group. Simultaneous treatment with lead and cinnamon oil in rats has shown that more time was spent in the open arms (50.0%) as compared to different doses of lead treated rats. Similarly, lead and vitamin-E treated rats have also caused more time spent in the open arms (37.9%) when compared to lead intoxicated rats (Figure 3).

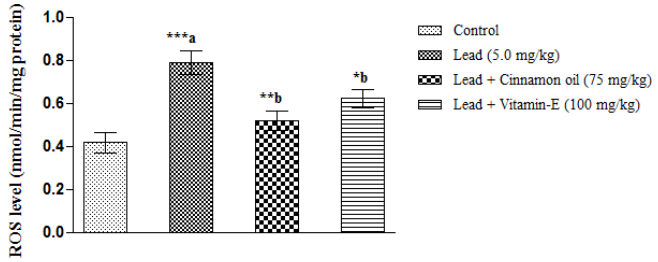


Values are mean ± S.E. (n=5). a***(P < 0.001)-compared to control group,b* (P < 0.05), b** (P < 0.01)-compared to lead treated groups

Figure 3. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-E on Elevated plus-maze test of rats for 28 days

Effect on reactive oxygen species

A significant increased level of ROS in brain (1.9 fold) was observed in rats by exposure to lead as compared to control. Rats treated simultaneously with lead and cinnamon oil caused decrease ROS level in brain (1.5 fold) as compared to rats treated with lead alone. Similarly, treatment with lead and vitamin-E in rats also exhibited decrease ROS level in brain (1.3 fold) as compared to rats treated with lead alone group (Figure 4).

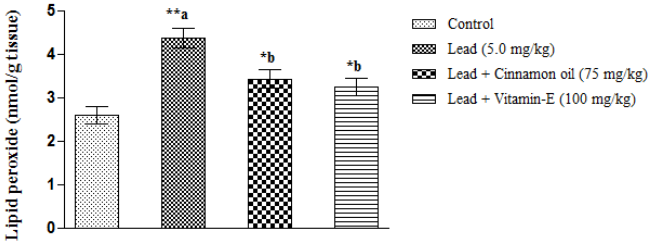


Values are mean ± S.E. (n=5). ***a (P < 0.001)-compared to control group, *b (P < 0.05), **b (P < 0.01)-compared to lead treated groups

Figure 4. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-Eon the levels of reactive oxygen species in brain of rats for 28 days

Effect on lipid peroxide

Lipid peroxidation level in brain (68.5%) was significantly increased in rats of lead treated group as compared to control. Co- treatment with lead and cinnamon oil exhibited significant decrease in LPO level (21.5%) as compared to rats treated with lead treated alone. Also, in lead and vitamin-E exposed groups significantly decreased LPO level (25.6%) was produced as compared to rats treated with lead alone group (Figure 5).

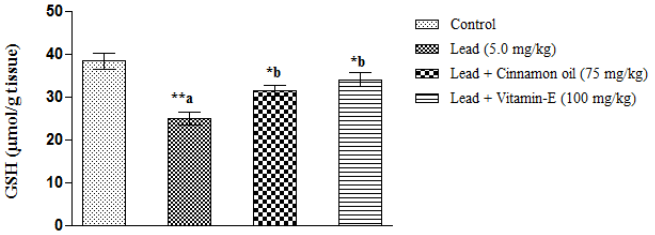


Values are mean ± S.E. (n=5).**a (P < 0.01)-compared to control group, *b (P < 0.05)-compared to lead treated groups

Figure 5. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-Eon the levels of lipid peroxide in brain of rats for 28 days

Effect on reduced glutathione

A significant decrease in the level of GSH in brain (35.0%) was observed in lead treated rats compared to that of control group. Rats exposed simultaneously with lead and cinnamon oil caused an increase in the GSH levels in brain (25.7%) as compared to rats treated with lead alone. Similarly, treatment with lead and vitamin-E in rats caused an increase in the level of GSH in brain (36.4%) as compared to lead alone group (Figure 6).

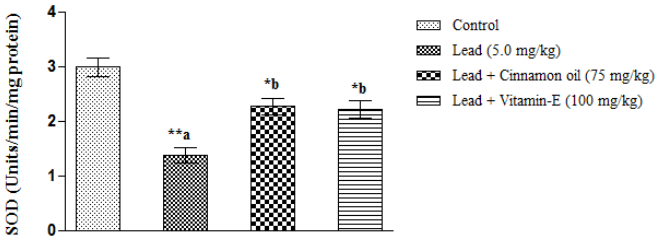


Values are mean ± S.E. (n=5).**a (P < 0.01)-compared to control group, *b (P < 0.05), **b (P < 0.01)-compared to lead treated groups

Figure 6. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-E on the levels of reduced glutathione in brain of rats for 28 days

Effect on superoxide dismutase activity

The activity of superoxide dismutase in brain (54.0%) of rats was significantly decreased in lead treated groups as compared to control. Simultaneous treatment with lead and cinnamon oil caused an increase in the activity of SOD (65.2%) when compared to lead treated rats. Similarly treatment with lead and vitamin-E in ratsalso exhibited an increase in the activity of SOD (60.9%) as compared to rats treated with lead alone group (Figure 7).

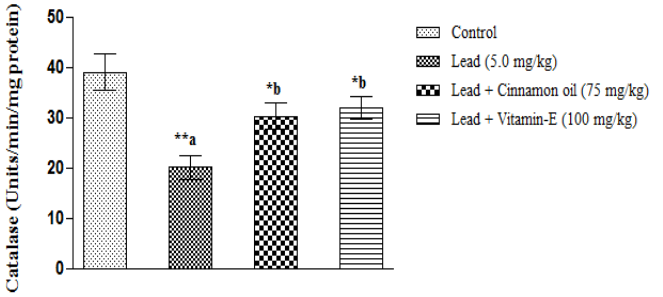


Values are mean ± S.E. (n=5). **a (P < 0.01)-compared to control group, *b (P < 0.05)-compared to lead treated groups

Figure 7. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-Eon the activity of superoxide dismutase in brain of rats for 28 days

Effect on catalase activity

Effect of lead on the activity of catalase in brain (48.4%)was significantly decreased in lead treated rats as compared to those of control. Rats exposed simultaneously with lead and cinnamon oil caused an increase in the activity of catalase (50.2%) as compared to rats treated with lead alone. Similarly, co-treatment with lead and vitamin-E in rats caused an increase in the activity of catalase (58.4%), when compared to rats treated with lead alone groups (Figure 8).

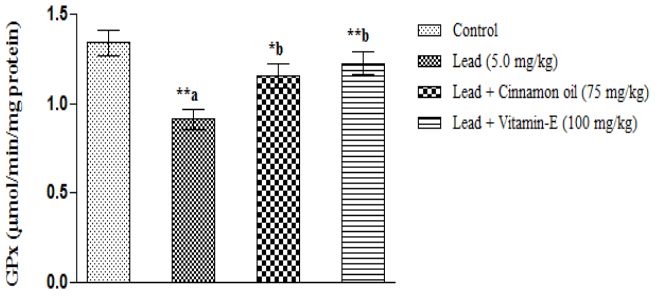


Values are mean ± S.E. (n=5).**a (P < 0.01)-compared to control group, *b (P < 0.05)-compared to lead treated groups

Figure 8. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-E on the activity of catalase in brain of rats for 28 days

Effect on glutathione peroxidase activity

Rats exposed to lead caused significant decrease in glutathione peroxidase activity (31.9%) as compared to those treated in the control. Simultaneous co-treatment with lead and cinnamon oil produced an increase in the activity of GPx (26.3%) as compared to rats treated with lead alone. Moreover, treatment with lead and vitamin-E inrats caused an increase in the activity of GPx (34.1%) in brain as compared to rats treated with lead alone (Figure 9).



Values are mean ± S.E. (n=5).**a (P < 0.01)-compared to control group, *b (P < 0.05), **b (P < 0.01)-compared to lead treated groups

Figure 9. Effect of Lead, Lead + Cinnamon oil and Lead + Vitamin-E on the activity of glutathione peroxidase in brain of rats for 28 days

Effect on lead level in blood and brain

As shown in Table 2. The levels of lead in blood (4.6 fold) and brain (3.8 fold) were significantly increased in rats treated with lead as compared to controls. However, levels of lead were found to be significantly reduced in blood (3.0 fold) and brain(2.3 fold) of rats exposed simultaneously with lead and cinnamon oil as compared to rats treated with lead alone groups. Similarly treatment with lead and vitamin-E in rats also caused a significant decrease in blood (2.1 fold) and brain (1.6 fold) as compared to those treated with lead alone groups.

Table 2. Effect of lead, lead + cinnamon oil and lead + vitamin-E on blood and brain lead level of rats for 28 days

Group	Blood Pb level (µg/dl)	Brain Pb level (µg/g wet tissue)
Control	6.60 ± 1.07	4.10 ± 0.43
Lead (5.0 mg/kg)	30.20 ± 1.56^{a,**}	15.40 ± 1.07^{a,**}
Lead + cinnamon oil (5.0 + 75mg/kg)	10.00 ± 1.71^{b,*}	6.60 ± 0.85^{b,*}
Lead + vitamin-E (5.0 + 100mg/kg)	14.10 ± 1.38^{b,*}	9.84 ± 0.98^{b,*}

DISCUSSION

Lead is one of the most common heavy metal, which is toxic to animals and humans. Lead crosses blood–brain barrier and disrupts its main structural and functional components by damaging the brain glial cells (Gandhi and Abramov,2012).It selectively deposits in brain and found to be associated with learning impairment, behavioral abnormalities, decreased hearing, impaired cognitive functions and neuromuscular weakness in humans and in experimental animals (Verina *et al*.,2007).It may also cause many biochemical changes and a variety of neurological disorders such as behavioral problems, mental retardation, nerve damage, Alzheimer's disease, schizophrenia and Parkinson's disease (Verina *et al*.,2007;Bazrgar *et al*., 2015).In our present study, lead exposure in rats caused behavioral impairments as compared to control. However cinnamon oil in combination with lead minimizes the effects of behavioral abnormalities, which was in agreement with the previous studies (Van den Berg *et al*.,1996).In particular, lead can cause major changes in the blood and brain and oxidative stress has been reported as a potential mechanism in the pathogenesis of its toxicity (Verstraeten *et al*.,2008).

The current study investigates the lead-induced oxidative stress and antioxidant ability of cinnamon oil in the blood and brain of rats, which were given lead exposure for 28 days. In the present study, lead exposure was associated with a decrease in the body weight and no significant change in brain weight as compared to control rats, which is in accordance with the previous studies (HyeJun *et al*., 2011). We have also observed the increased levels of lead in the brain which fur thergives indication that lead can cross blood-brain barrier and produces its toxic effects. The lead levels in the blood and brain of the lead treated group were significantly increased in comparison to control group. However, a decrease of lead level in blood and brain was shown in the lead plus cinnamon oil and lead plus vitamin-E treated rats. The toxic effects of lead may be due to its interference with calcium in activation of protein kinase C (PKCs) or through production of ROS. Lead competes with calcium for common binding sites and is mentionedin calcium transport systems of the nervous system (Devi *et al*., 2005). Oxidative damage is considered a major cause of lead-induced brain damage, because the brain is believed to be particularly vulnerable to oxidative stress due to the high rate of free radical generation without adequate levels of antioxidant defences (Adhami *et al*., 2000; Villeda-Hernandez *et al*., 2001). In vitro and in vivo studies state that lead exposure may cause the generation of ROS and changes in the antioxidant defense systems in animals (Nuran Ercal *et al*., 2001; Ahmed *et al*., 2012). Antioxidant enzymes such as SOD, CAT, GPx, and GR are supposed to be the primary defenses that prevent biological macromolecules from oxidative damage. Moreira *et al*. confirmed that brain antioxidants (SOD

and GPx) from individuals treated to lead decreased significantly (Moreira *et al*., 2001; Ahmed *et al*., 2012).

In the present study, SOD and CAT activity tends to decrease in the brain after lead exposure as compared to control group, whereas in simultaneously treated lead plus cinnamon oil and lead plus vitamin-E groups have shown increase in this parameter as compared to lead exposed groups. Wang *et al*. described that the GPx activity of mouse brain was decreased in the Pb-exposed group as compared with the control group (Wang *et al*., 2006). In present study similar results were found in GPx activities of lead-exposed group which decreases as compared to control groups and simultaneously increases in both, lead plus cinnamon oil and lead plus vitamin-E exposed group respectively, as compared to lead exposed groups. We also observed a significant decrease in the level of GSH in brain of lead exposed group as compared to the control, and an increase in the GSH level occurred in the both, lead plus cinnamon oil and lead plus vitamin-E exposed group. This study was in agreement with previous studies (Aykin-Burns *et al*., 2003). A number of in vitro and in vivo studies have shown that a significant increase of the LPO level is correlated with an increase in the lead exposure (Yiin and Lin, 1995). In our study, we also observed increase lipid peroxidation level in the brain after exposure to lead as compared to control. However, the LPO level of rats that were simultaneously treated with lead plus cinnamon oil and lead plus vitamin-E respectively, was significantly decreased compared to the Pb-exposed group. Flora *et al*., 2007 reported that delta amino levulinic acid caused ROS generation which may be one of the factors contributing to oxidative stress due to lead exposure. A significantly increased ROS level in lead exposed animals in our study as compared to control, which is in accordance with previous studies. Rats exposed simultaneously with lead plus cinnamon oil and lead plus vitamin-E also exhibited decrease in ROS level in brain as compared to rats treated with lead alone. In fact, few studies have investigated the molecular and biochemical mechanisms by which cinnamon exerts neuro protective action and the therapeutic potential of cinnamon oil in ameliorating the risk factors liable for the development of neurodegenerative diseases and associated pathologies (Stavinoha and Vattem, 2015).

Conclusion

We can conclude from the results obtained from this study that lead which induces oxidative stress and behavioral impairment in rats is one of the dangerous heavy metals. Cinnamon oil has been found to attenuate the lead induced oxidative stress which may be due to its chelating properties. An increase of antioxidant activities and decrease of oxidative stress, improvement in behavioral abnormalities in animals given cinnamon oil simultaneously with lead exposure was also shown. Therefore cinnamon oil seems to protective against lead induced neurotoxicity. Finally our result suggested that cinnamon oil may play a protective role in lead induced neurotoxicity and associated human health risk. Furthermore, long studies in animals and clinical studies in lead exposed human beings are required to strengthen our present study**.**

Acknowledgements

The authors highly thankful to Dr. Talha Jawaid (Head, Department of Pharmacology, Hygia Institute of Pharmaceutical Education and Research, Lucknow)for their valuable suggestions. We also extend our sincere thanks to Late Dr. Ramesh Chanderretired Scientist F, CDRI, Lucknow and Mr. Sushil Verma, who were always a source of knowledge and inspiration and technical staff for their dedicated support, kind nature, valuable suggestions and encouragement in times of difficulties during research.

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