Beneficial effect of vitamin-E and–C supplementation on oxidative damage and total antioxidant capacity in lead exposed workers

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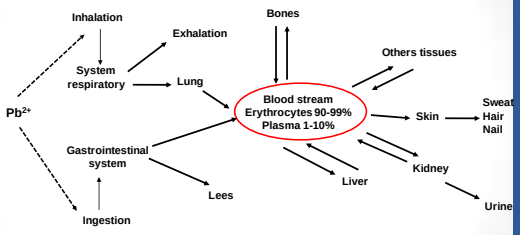
Lead is one of the most commonly used metals in industry.
Lead toxicity is a public health problem due to lead-environmental persistence, poor security condition and low lead excretion in lead-exposed workers.

Exposure to lead can result in significant alterations in multiple organs.



The hematological system is an important target and the erythrocytes have a high affinity for lead and typically contain a majority of the lead found in the blood stream.

Nilsson U, et. al.. Pharmacol Toxicol 1991; Calderón-Salinas JV, et.al Human Exp Toxicol 1996; Bleecker ML, McNeill FE, Lindgren KN, Masten et. al. Toxicol Lett 1995; 77: Ehrlich R et. al, Occup Environ Med 1998: Levin et. al.. Am J Ind Med 2000, Patrick L. et. al.Altern Med Rev 2006.Quintanar-Escorza MA, et. Toxicol Appl Pharmacol 2007.

Clinical symptoms and signs of lead intoxication

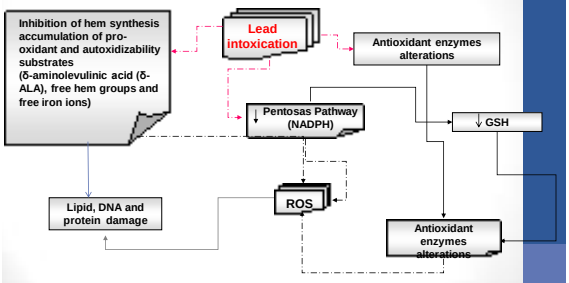
The toxic mechanisms of lead on the molecular machinery of living organisms are caused by:

Covalent binding to proteins
Simons,British Medical Bolletin, 1986 .Goering PL, 1993. NeuroToxicology 14:45-60.Thomas DM. 2003.Salud Pública México. 45 supl 2:S220-S224.

Interaction on stereospecific sites for divalent cations such as Ca^{2+}, Zn^{2+}, Cu^{2+}
Fukumoto K, et al.,1983. British Journal of Industrial Medicine.Garza Al et al. 2006. Medical Science Monitor .RA57-65. 1Calderon-Salinas JV et al. Human Experimental Toxicology. 1999.

Damage oxidative.
Chiu, Bull Environ Contam Toxicol, 1997, Bjorneboe,Bristish Journal of industrial Medicine, 1990 .`Carter DE. 1995. Health Perspectives. Vol.103 (suppl 1):1.Adonaylo VN et al 1999. Toxicology. 1Gurer-Ohrnan H et al. 2004. Toxicology. Flora SJ, et. al Indian J Med Res 2008

Lead intoxication is involved in many oxidative insults within the organism; several studies suggest the involvement of oxidative damage in lead toxicity mechanisms

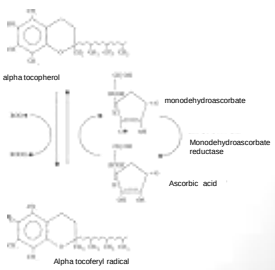


Cimen MY. Clin Chim Acta 2008; Dröge W.et.al Physiol Rev 2002; Valko M, et. al. J. Int J Biochem Cell Biol. 2007; Auten RL et al.. Pediatr Res 2009; Kasperczyk S, et.a al Ann Agric Environ Med 2004; Kasperczyk S, et. al. Biol Trace Elem Res Winter 2004.

Few studies have been carried out to evaluate the beneficial effects of exogenous antioxidant treatment in lead intoxicated workers.

In lead-exposed workers, treatment with vitamin C, vitamin E, beta-carotene, selenium, zinc or chromium was been able to reverse the inhibition of δ-aminolevulinic acid dehydratase (δ-ALAD) activity in blood, increasing the total antioxidant capacity (TAC) and SOD and GPx activity, while abating the toxic effects associated with inhibition of the calcium pump
Tandon SK et.al *Sci Total Environ* 2001; Machartová V, et al. *Vnitr Lek* 2000; Abam E, et. al. *Environ Toxicol Pharmacol* 2008.

Vitamin E is a lipid soluble non-enzymatic antioxidant, vitamin C is an aqueous antioxidant. Simultaneous administration of vitamins E and C is particularly interesting due to the regeneration of the enzymatic system having been found to be more effective in reducing the oxidation manifestation during concomitant administration.
Traber MG, et. al. Free Radic Biol Med 2011; 51: 1000-13.



MATERIALS AND METHODS

Subjects
Two groups of workers located in León, Guanajuato, Mexico, were studied.

One group consisted of 15 male workers who were occupationally exposed to lead in a recycling battery factory, particularly to the dust of a mixture of lead oxides. The other group (control, non-lead exposed) consisted of 19 male volunteer workers without history of occupational lead exposure and clinically healthy. To confirm this, healthy volunteers were evaluated with routine analysis of blood and urine, showing normal parameters.

Exclusion criteria:
History of or current physical findings of serious neurological, cardiovascular, renal, hepatic, endocrine, metabolic or gastrointestinal disease; and no previous pharmacological treatment. All subjects provided written, informed consent and participation was voluntary.

The study was approved by the Medical Center-Bajio, IMSS-Mexico.

Both groups had similar age, non-lead exposed 35 ± 5 years and lead-exposed 33 ± 8 years old and with comparable socioeconomic and nutritional conditions

Socio-demographic characteristics and clinical symptoms and signs of lead intoxication in non-lead exposed and lead exposed workers.

	Non-lead exposed (n=19)	Lead exposed (n=15)
Gender	Masculine	Masculine
Age (years)	35 ± 5	33 ± 8
Social position score (index)	92 ± 8	85 ± 6
Lead exposition time (years)	-----	6.0 ± 4.0*
range (-)		(8 – 12)
Clinical symptoms and signs of lead intoxication		
Dizziness (%)	5.3	46.7**
Headache (%)	15.8	66.7**
Paresthesia (%)	5.3	40.0**
Paresis (%)	0.0	20.0**
Abdominal colic (%)	10.5	33.4**
Myalgia (%)	10.5	53.4**
Motor coordination alteration (%)	5.3	93.3**

Values are mean ± SD.*Significant difference (P ≤ 0.05) as compared to non-lead exposed workers, **Significant difference (P ≤ 0.05) as compared to non-lead exposed workers, according to X2 test. Each subject received two capsules per day for a period of 12 months (vitamin E 400 IU and vitamin C 1 g). Patients were instructed to take the capsules with breakfast meals into their workplace.

Biological indices of lead intoxication and antioxidant defense system and lipid peroxidation status in blood of non-lead exposed and lead exposed workers.

	Non-lead exposed (n=19)	Lead exposed (n=15)	
PbB (µg/dl)	6.7 ± 2.2	73 ± 20*	↑ 10.9 times
δ-ALAD activity (nmol PBG/h/ml)	683 ± 61	138 ± 43*	↓ 79.8%
TBARs (nmol MDA/ml PG)	0.74 ± 0.26	1.3 ± 0.31*	↑ 75%
TAC (1/(FUA/5x10⁵ cells))	66 ± 3.7	109 ± 8.0*	↑ 40%
Enzymatic activity (U/g Hb)	Non-lead exposed (n=19)	Lead exposed (n=15)	
CAT	10 ± 1.9	37 ± 8.9*	↑ 3.7 times
SOD	202 ± 61	534 ± 51*	↑ 2.6 times
GPx	12 ± 1.5	10 ± 2.5	
GRx	9.7 ± 1.4	3.1 ± 1.2*	↓ 68%
Serum concentration			
Vitamin E (µmol/l)	24 ± 5.8	22 ± 4.2	
Vitamin C (µmol/l)	69 ± 8.9	71 ± 8.8	

Blood lead concentration (PbB), aminolevulinic acid dehydratase activity (δ-ALAD), total antioxidant capacity (TAC) and thiobarbituric acid reactive species concentration, (TBARs). Values are mean ± SD.*Significant difference (P ≤ 0.05) as compared to non-lead exposed workers.

Effects of vitamin E/ vitamin C supplementation on levels of biological indices of lead intoxication and oxidative stress in blood of non-lead exposed and lead exposed workers.

	Non-lead exposed (n=19)		Lead exposed (n=15)	
	Before	After	Before	After
PbB (µg/dl)	6.7 ± 2.2	7.1 ± 1.4	73 ± 20	69 ± 17
δ-ALAD activity (nmolPBG/h/ml)	683 ± 61	696 ± 51	138 ± 43	315 ± 24*

Figure 2A

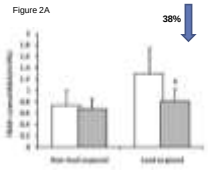
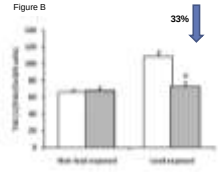


Figure B



Blood lead concentration (PbB) and d-aminolevulinic acid dehydratase activity (d-ALAD), before and after supplementation. A) Lipid peroxidation (TBAR`s) and (B) total antioxidant capacity (TAC) before and after vitamin E/vitamin C supplementation in blood of non-lead exposed and lead exposed workers. Values are mean ± SD. *Significant difference (P≤0.05), before supplementation according to ANOVAs test.

Effect of vitamin E/vitamin C supplementation on the antioxidant status in blood of non-lead exposed and lead exposed workers

	Non-lead exposed (n=19)		Lead exposed (n=15)	
	Before	After	Before	After
Serum vitamin E (µmol/ml)	24 ± 5.8	51 ± 5.7*	22 ± 4.2	26 ± 7.2
Serum vitamin C (µmol/l)	69 ± 8.9	104 ± 9.5*	71 ± 8.8	88 ± 8.4
GPx activity (U/g Hb)	12 ± 1.5	14 ± 1.8	10 ± 2.5	10 ± 3.1
GRx activity (U/g Hb)	9.7 ± 1.4	11 ± 1.5	3.1 ± 1.2	3.9 ± 1.0

Figure A

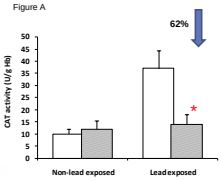
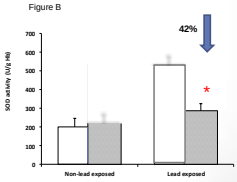


Figure B



CAT activity and SOD activity, before and after vitamin E/vitamin C supplementation in erythrocytes of non-lead exposed and lead exposed workers. GPx activity, GRx activity, serum vitamin E concentration, plasma vitamin C concentration in blood of non-lead exposed and lead exposed workers, before and after supplementation *Significant difference (P ≤ 0.05), before supplementation according to ANOVAs test.

CONCLUSIONS

- **The lead intoxication was accompanied by a higher oxidative damage (75%) and this was attenuated by an increment in the erythrocyte antioxidant response (40%) due to increases of catalase and superoxide dismutase activities (3.7 and 2.6 times higher respectively).**
- **The antioxidant supplementations decrease significantly the oxidative damage (38%) as well as the total antioxidant capacity (33%) induced by lead intoxication.**
- **Additionally, vitamin E and C supplementation reduced the antioxidant enzymes activities (catalase 62% and dismutase superoxide 42%).**
- **Hence, the antioxidant supplementation is effective to reduce oxidative damage and to induce modification in the physiopathological status of the antioxidant response in lead-exposed workers.**