J. Mountain Res. P-ISSN: 0974-3030, E-ISSN: 2582-5011 DOI:https://doi.org/10.51220/jmr.v17i2.22
Vol. 17(2), (2022), 199-204

Hepatoprotective Effect of Vitamin-E (α-Tocopherol) on Trichloroethylene and Toluene Induce Liver Damage in Rats

Sujata Gupta[1*] • Dharmendra Kumar[2] • JVS Rauthan[3] • Barkha Kamal[4]
[1]*Department of Zoology, D.A.V. (P.G.) College, Dehradun-01, Uttarakhand, India*
[2]*Department of Zoology, S.V.P.G. College, Lohaghat. Uttarakhand, India*
[3]*Department of Zoology, D.A.V. (P.G.) College, Dehradun-01, Uttarakhand, India*
[4]*Department of Botany, D.B.S. (P.G.) College, Dehradun-01, Uttarakhand, India*
***Corresponding Author Email id**: sujatadavpg@gmail.com

Received: 19.09.2022; Revised: 10.10.2022; Accepted: 26.10.2022

Abstract: This study was design to investigate the harmful effect of trichloroethylene and toluene on the hepatic cell of rats and possible protective effect of vitamin-E (α-tocopherol) on these detrimental effects. This study aimed to evaluate organic solvents which are persistent and uninterrupted ecological pollutants that are capable to cause numerous dysfunctions in target tissues of exposed animal as well as humans. This study suggests that trichloroethylene (TCE) and toluene when administered in rats changes their metabolic disposition. Therefore, investigation work performed as to (a) Compare the rate of lipid peroxidation in hepatic tissues, (b). To study the concomitant effect on reduced glutathione in liver of rats subjected to TCE and toluene with vitamin-E (VE) to protect the damage of liver cells.

Keywords: Vitamin-E • Lipid-peroxidation • Glutathione • Trichloroethylene • Toluene

Introduction

Organic solvent are environmental toxicant and impacting negative health effects and over all well being of exposed individual. Recently industrial activities have been rapidly increased which leads to prolong direct or indirect exposure of various organic solvents in humans, which may be exposed during manufacture, handling and transport etc.

Trichloroethylene is an occupational and environment contaminant, which produces and applies on huge scale and after use discarded inappropriately (Hurzmann, et al 2020). The primary sources of trichloroethylene release into the environment are metal cleaning and decreasing operations, (Wu and Schaum 2000). These type of organic solvents are well known carcinogens and associated with several toxic effect including immunotoxicity, hepatic-toxicity, neurotoxicity and even nephrotoxicity, (Huang2021). Neurodegenerative changes due to organic solvent also reported by (DeMiranda and Green mayor 2020). Trichloroethylene is a chlorinated hydrocarbon and not found in natural habitat even though it could be detectable in underground and surface water (Gilbert etal, 2017) generally human population exposed through transdermal absorption, inhalation and ingestion.

Toluene is a highly toxic and lethal compound to mammals (Pelletti etal 2018). Toluene is a good solvent for some types of paint thinner, permanent markers, contact cement and certain types of glue; toluene is sometimes used as a recreational inhalant (McKeown NJ, 2015), and has the potential of causing severe neurological harm. Organs like liver and kidney being extremely sensitive to the toxic affects of xenobiotics agents viz toluene and other harmful chemicals, due to the presence of high detoxifying, degrading and bio activation enzymes of these organ to metabolize xenobiotics compounds (Nigam, etal 2021). Cytochrome P450 enzymes primarily present in hepatic cell which is responsible for the

metabolism of the xenobiotics in the organ (Wu, et al 2021).

The liver plays a key role in transforming and clearing chemicals and is susceptible to the toxicity from these agents. When these chemical or agents enter in the body and causes dysfunction in hepatic cells is known as hepatotoxic. The liver is the chief target organ for the xenobiotic compounds like toluene and trichloroethylene toxicity. Hepatic cells when exposed to various stimuli, such as the extensive destruction of hepatic tissue by toxins, viruses, or even surgical removal, exhibit a very good regeneration response. The liver's coordinated and controlled reaction to tissue damage brought on by toxic or chemical agents causes oxidative stress in the liver and it leads to the regeneration of the liver tissues (Rabelo etal, 2006). Vitamin-E is fat soluble vitamin recognised as essential nutrient for all living species of animals and human and it plays a magnificent role as most powerful antioxidant of lipid membrane. Antioxidant may prevent or delay some type of cell damage. When human body exposed by several pollutants, free radicals (FR) are formed. These free radicals are highly reactive and unstable compound they can damage DNA and cause in health effect and even mutation. Antioxidant can neutralize these unstable molecules and reduce the chance of cell damage by them.

Materials and methods:

Animal: 4-month-old male Wistar rats were selected for this investigation. They were acclimatized individually for 10 days, in polypropylene cages under standard laboratory condition (R.T.25+_50C, R.H.50+10%) and fed on the diet following the guideline of NIH (USA).

Experimental protocol: Rats were divided into 5 groups. Each group contained sufficient no. of rats, so as to get statistically valid results. (Table 1).

Table 1: Experimental Protocol

Group	Treatment	No. Of Rats Employed (Male)	Dose Administered/ 100gm Body Weight	Vehicle /Route	Treatment Duration
A	TCE	05	0.5ml	Olive Oil Intra peritoneal	Each Alternate Day for 30 days
B	TCE + Vitamin-E	05	0.5ml	-do-	-do-
C	Toluene	05	0.5ml	-do-	-do-
D	Toluene + Vitamin-E	05	0.5ml	-do-	-do-
E	Control: Olive Oil	05	0.5ml	-do-	-do-

Analysis:

After the treatments all the experimental rats were starved overnight and sacrifice next morning by the decapitation. Pieces of liver were quickly removed and process for the Malondialdehyde estimation by Thiobarbituric acid (Wako Japan method), 1.1.3. -Tetramethoxypropane (Japan Wako) was used as standard. Reduced glutathione (GSH) was using 5, 5 dithiobis-2 nitrobenzoic acid (Sigma USA). Protein was estimated by Lowry method (Lowry etal, 1951). Inter group comparison were made using student t- test.

Results and Discussion

Table 2: Protective effect of Vitamin-E on Lipid Peroxidation in Rats' Liver Treated with TCE & Toluene

Group	Treatment	MDA in Liver (n-mole/ mg protein)
A	TCE	0.181±0.032[b]
B	TCE + Vitamin-E	0.175±0.042[a]
C	Toluene	0.248 ± 0.050
D	Toluene + Vitamin-E	0.199 ± 0.031
E	Control: Olive Oil	0.146 ± 0.002

Values are mean ± SE of 05 observations in each group of rats P value a<0.01: b<0.02

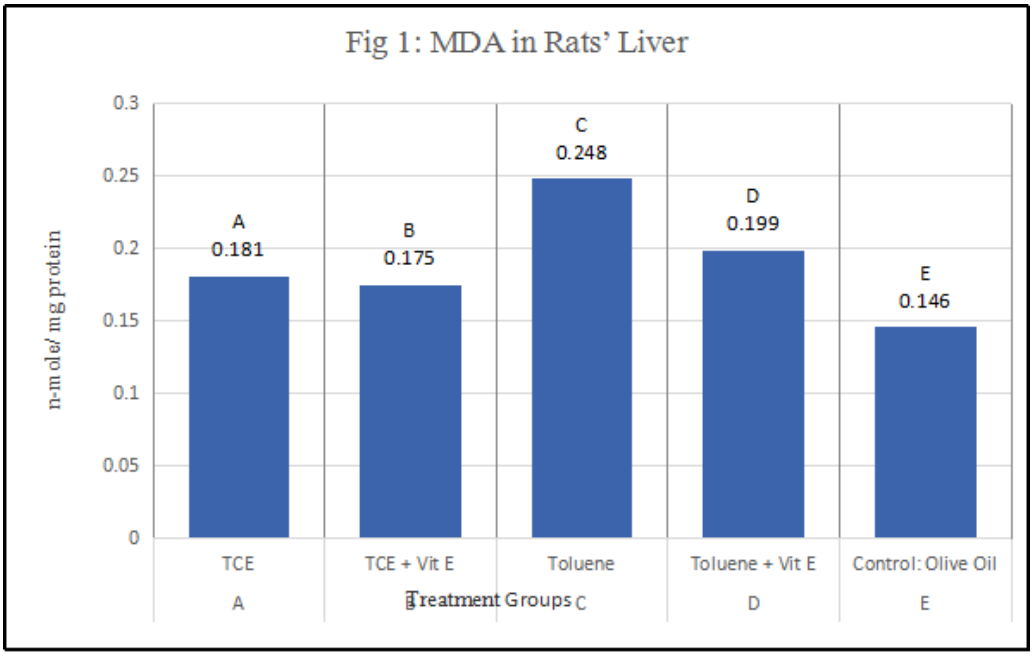
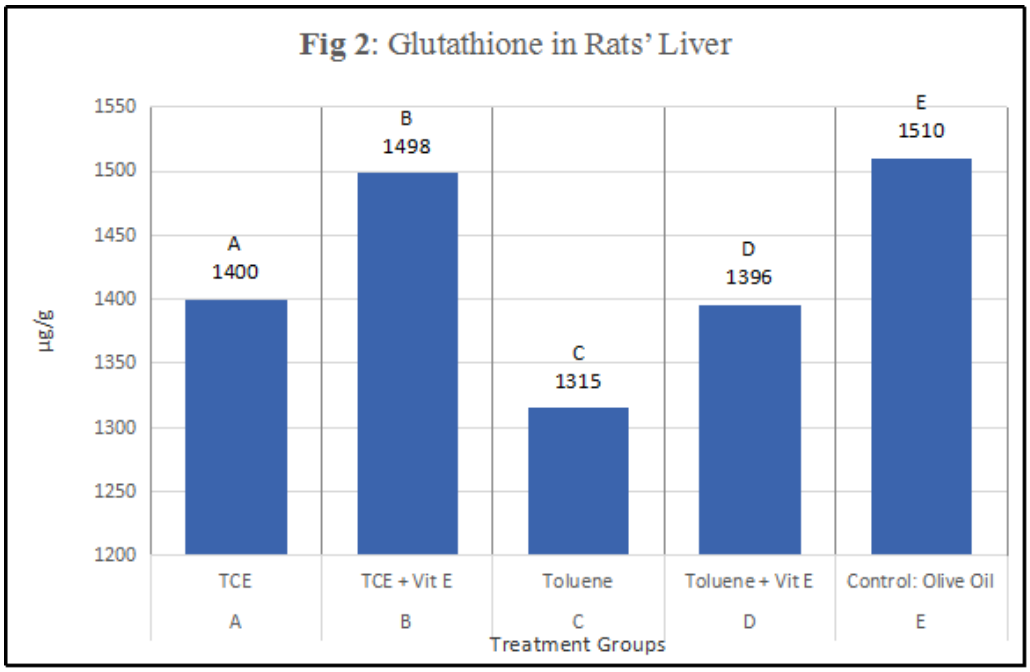


Table 3: Protective Effect of Vitamin-E on Glutathione in Rats' Liver Treated with TCE & Toluene

Group	Treatment	Liver GSH (µg/g)
A	TCE	1400 ± 4.68
B	TCE + Vitamin-E	1498 ± 10.26[a]
C	Toluene	1315 ± 8.08[a]
D	Toluene + Vitamin-E	1396 ± 3.68
E	Control: Olive Oil	1510 ± 4.69

Values are mean ± SE of 05 observations in each group of rats P value a<0.001



Per-oxidation of the membranous lipid was higher in the liver of toluene treated and followed by trichloroethylene treatment however, formation of Malondialdehyde decrease with comparison of vitamin-E simultaneously treated rates. Malondialdehyde (MDA) is most determinant biomarker for detection of lipid peroxidation or pathogenesis of tissue by any toxic substances if value of MDA increase it indicates injury in cell membrane or variety of chronic disease both animals and humans (Table 2).

Increase in lipid peroxidation corresponded with glutathione depletion. Hepatic injury by trichloroethylene and toluene has been a controversial issue. (Rana and Sunil 1994).

According to previous research, the primary cause of the cell damage caused by aromatic organic compounds is because of the covalent binding of their reactive metabolites to macromolecules. Oxygen species so produced create oxidative stress and which ultimately results in lipid peroxidation. GSH (Glutathione) is important antioxidant and protects cells against oxidative injuries by reducing H_2O_2 and scavenging reactive oxygen and nitrogen radicals. As our results shows that values of GSH decrease, in rats treated with trichloroethylene and toluene alone when TCE and toluene injected with vitamin E value level of GSH increases Table(3). GSH is essential for normal function and survival of cells, as one of the principal reducing molecule in the hepatic cells. Redox state of sulfhydryl group of cellular protein is regulated by GSH by virtue of its major antioxidant property. It fights with exogenous oxidative stress and captures endogenous species. When we give Vitamin-E to rats, there is changed in liquid peroxidation and GSH observations. It shows that vitamin E has the ability to reverse or prevents chemical induced hepatotoxicity as also reported earlier (Khalifa et al, 2009).

Disordering of GSH, liver homeostasis not only causes ROS production that oxidise protein, lipids and DNA, but also effect several signalling pathways and thus affects intermediary metabolism, proliferation and survival. As a result liver dysfunction and various pathologies of liver may occur.

Vitamin-E, inhibits membranous lipid peroxidation, but enhances GSH values by means of two mechanisms, on one side it eliminates the free radicals that produces during lipid peroxidation and inhibit the

oxidation chain reaction and on other side it acts as a singlet oxygen chelator. Vitamin-E ruptures the oxidation chain that prevents the propagation of free radical in reactions. This protect cell from oxidative stress. Particularly vitamin-E is an important cell protector against lipid peroxidation during which free radicals attack the unsaturated fatty acids, which result structural damage to the membrane and form secondary cytotoxic products such as MDA among others (Jervis and Robaries 2004).

Conclusion

Our finding reflects the hepatotoxicity of these two organic solvents which may be attributed to increase the generation of free radicals and disturbance of antioxidant enzymes. This finding indicates that addition of vitamin-E was efficacious in decreasing of lipids peroxidation by lessening the oxidative stress and elevating glutathione level.

This shows that vitamin-E behaves as a free radical scavenger and can give an effective protection to both animals and humans by reducing damage due to oxidative stress and hepatotoxicity in industrial workers. Thus, we recommend more experimental and clinical studies to confirm the efficacy of Vitamin-E in treating xenobiotic-induced toxicity due to oxidative stress damages.

References

De Miranda BR, Greenamyre JT., (2020). Trichloroethylene, a ubiquitous environmental contaminant in the risk for Parkinson's disease. Environ Sci Process Impacts 22:543–554. https://doi.org/10.1039/ c9em00578a

Gilbert K.M., Bai S., Barnettle D., (2017). Exposure cessation during adulthood did not prevent immunotoxicity caused by development exposure to low level TCE in drinking water. Toxicol. Sci: 157(2): 429-437.

Horzmann KA, Portales AM, Batcho KG, Freeman JL., (2020). Devel- opmental toxicity of trichloroethylene in zebrafish (*Danio rerio*). Environ Sci Process Impacts 22:728–739. https://doi.org/10.1039/ c9em00565j

Huang Y, Xia Y, Tao Y, Jin H, Ji C, Aniagu S, Chen T, Jiang Y., (2021). Protective effects of resveratrol against the cardiac developmental toxicity of trichloroethylene in zebrafish embryos. Toxicology 452:152697. https://doi.org/10.1016/ j.tox.2021. 152697

Jervis K. and Rabaire B., (2004). The effect of long-term vitamin E treatment on gene expression and oxidative stress damage in ageing brown Norway rats epididymis. Biology of Reproduction. Vol. 71 pp 1018-1095 ISSN 0006-3363.

Khalifa M.A., V. Maksymov and C. Rowsell, (2009). Retroperitoneal margin of the pancreaticoduodenectomy specimen: Anatomic mapping for the surgical pathologist. Virchows Arch, 454: 125-31. PMID: 19066952

Lowry, O.H., Rosenbrough, N.J., Farr, A.L.and Randall (1951). J.Biol. Chem. 193.265.

Mc Keown N J., (2015). Toluene toxicity, Background, Pathophysilogy, Epidemology web med professional Network.

Nigam A.K., A.A. Ojha, J.G.LI, D.Sh., V.Bhatnagar, K.B.Nigam., (2021). Molecular properties of drugs handled by kidney OATs liver OATs revealed by chemo informatics and machine learning: implications for liver and kidney diseases. Pharmaceutics 13, 1720.

Pelletti G, Rossi F, M.Garagnani, R.Barone, R. Roffi., (2018). Medico-legal implications of Toluene abuse and toxicity. Review of case along with blood concentrations. Leg.Med.34, 48-57.

Rabelo, M.R., F.S. Ramalho, L.N. Ramalho, S.C. Tde and D.F. Brandao et al.,(2006). A molecular view of liver regeneration.

Acta Cir. Bras., 21: 58-62. PMID: 17013516

Rana SVS and Kumar Sunil, (1994). Lipid peroxidation in liver, kidney and brain of rats combined exposure of xylene, toluene and methyl alcohol. Indian Journal of Expt. Biology. vol 32, 919-921

Wu C, Schaum J., (2000). Exposure assessment of trichloroethylene. Environ Health Perspect 108:359–363. https://doi.org/10.1289/ ehp.00108s2359

Wu KL, Berger T., (2008). Ovarian gene expression is stable after exposure to TCE. Toxicol Lett. 177(1) 59-65.

Wu X., Y.Chen, X.Wang, W.Wei, Y.Liang., (2021). Origin of site selective in toluene hydroxylation by cytochrome P450 enzymes. J.Org. Chem, 86, 13768-13773.