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Vitamin E Modulates the Oxidant-Antioxidant Imbalance of BPA induced Oxidative Stress in Albino Rats

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Abstract: ***Bisphenol A (BPA) is one of the world's highest production volume chemicals used in polycarbonate plastics in many consumer products and epoxy resins lining food and beverage containers. Study on the oxidative stress and antioxidant enzyme defense system in BPA induced rats blood sample revealed an augmented oxidative stress due to BPA level in rat blood sample and decreased antioxidant enzyme defense which might decrease the blood pumping efficiency and leading to the probable increase of oxidative stress in blood. the supplementation of vitamin E is an important lipid soluble antioxidant invivo, and it is presumed that its principle role is to protect membrane lipids from lipid peroxidation invivo, by scavenging lipid alkoxy or peroxy radicals which are capable of abstracting hydrogen from adjacent polyunsaturated lipid molecules to propagate a lipid peroxidation reaction and thus prevent the serum damage due to oxidative stress.***

Keywords: Oxidative stress, BPA, Vitamin E, Antioxidants

1. Introduction

Oxygen as an essential element is critical for energy production and existence of all organisms on earth. However, there are potentially damaging effects also associated with it leading to production of oxygen centered free radicals. These radicals are highly reactive and can cause damage to various biomolecules. Presence of a physiological antioxidant defense system keeps these free radicals in check. Any imbalance in the levels of free radicals or reactive oxygen species (ROS) leads to oxidative stress in the body and may culminate in various patho-physiological conditions.

In recent years, considerable attention has been focused on endocrine disrupting compounds and their impacts on the environment and human health, raising questions about their levels of exposure. Bisphenol A (BPA) is one of the world's highest production volume chemicals (Ritter 2011) used in polycarbonate plastics in many consumer products and epoxy resins lining food and beverage containers (EU 2008). BPA is a kind of potential endocrine disruptor. It is a ubiquitous xeno estrogen that can leach into the contents during processing and storage. Moreover, BPA–based resins are commonly used in dentistry. Therefore the Human population is continuously and inevitably exposed to low doses of BPA in daily life. Importantly, BPA has been detected in amniotic fluid, cord blood and human breast milk, which demonstrates the potential of this compound to pass from mother to fetus. Evidence suggests that conditions experienced during early development play an important role in determining the long term health of individuals.

The global population is subjected to repeated exposure to BPA, primarily through packaged food but also through drinking water, dental sealants, dermal exposure and inhalation of household dusts (Lakind and Naiman 2008) with detectable concentration of metabolites in the urine of >90%of the population worldwide (Calafat *et al.* 2005; Ye *et al.* 2008). Heat, repeated washing of polycarbonate products and contact with either acidic or basic compounds accelerate hydrolysis of the ester bond linking BPA molecules in polycarbonate plastics and resins resulting in an increase in the rate of leaching of BPA (Lim *et al*.2009). In addition, another potential source of human exposure is water used for drinking or bathing. Studies conducted in Japan (Kawagoshi *et al*.2003) and in the united (coors *et al*.2003) shown that BPA accounts for most estrogenic activity that leaches from landfill into the surrounding ecosystem.

Increasing evidences shows that adverse effect of BPA on health are miscellaneous, varying with duration, doses and route of BPA Exposure, as well as sex difference. In humans, increased levels of BPA in adults have been correlated with various diseases, health outcomes and medical conditions. To date, reported health complications associated with increased level of BPA exposure include diabetes (Lang *et al*.2008), cardio vascular diseases (Lang *et al*.2008; Melzer *et al*.2010) altered liver enzymes as increase in alanine amino transferase and aspartate aminotransferase (Lang *et al*.2008;mourad and khadrawy 2012) and obesity promoting effects (Ropero *et al*.2008, tracavengesande *et al*.2012;Harley *et al*.2013) contributing to the potential for altered metabolic homeostasis, BPA has been shown alter glucose homeostasis, increase pancreatic insulin content and induce insulin resistance in adult male mice (Alonso-magdalena *et al*.2006).

BPA can cause liver, kidneys, brain, and other organs injury by forming Reactive oxygen species (ROS). ROS are

cytotoxic agents causing oxidative damage by attacking cell membrane and DNA. The liver has a range of antioxidant defense system. ROS are scavenged by the endogenous antioxidant defense system, including superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) in cells. When the capacity of this antioxidant system decreases, the level of inactivated ROS rises.

Reactive oxygen species (ROS) are involved in the pathogenesis of several diseases and tissue damages (Slater ***et al***. 1987; Wei, 1998; Lee ***et al.*** 1999; Calabrese ***et al***. 2005).These reactive species include superoxide anion ($O_2^{\cdot}$), hydrogen peroxide (H_2O_2) and hydroxyl radical (·OH). ROS may cause cell injuries such as lipid peroxidation, enzyme inactivation, changes in intracellular redox state and DNA damage (Halliwell and Gutteridge 1985; Bejma and Ji, 1999; Zhang **et al**. 2005; Rubio-Gayosso ***et al***. 2006). Oxidative stress can be defined as state of disturbance in the proxidant/antioxidant balance in favour of the former leading to potential damage. Cells possess enzymatic defense system to reduce the risk of oxidative injury to the cells that can cause cellular malfunction and even cell death.

Vitamin E (α- tocopherol) is considered one of the most important dietary antioxidant in biological systems due to its association with cell membrane and its ability to act directly on reactive oxygen species (ROS) preventing peroxidation. Besides the well characterized function of vitamin E as antioxidant alternative roles such as that of a membrane stabilizer, and a regulation of membrane fluidity have been proposed. The protective role of vitamin E on the oxidative stress develops due to antileprosy chemotherapy in leprosy patients was recorded. In the present study is carried out to evaluate the impact of vitamin E supplementation on the oxidative stress during BPA administration.

Vitamin E (α-tocopherol) is considered one of the most important dietary antioxidant in biological systems due to its association with cell membrane and its ability to act directly on reactive oxygen species (ROS) preventing peroxidation (Burton and Traber 1990; Azzi ***et al***. 2000; Xu ***et al***. 2003; Kir ***et al***. 2005). Besides the well characterized function of vitamin E as antioxidant alternative roles such as that of a membrane stabilizer (Urano ***et al.*** 1989; Kim, 2005) and a regulation of membrane fluidity (Ohyashiki ***et al.*** 1986; Ohyashiki ***et al***. 1998) have been proposed. The protective role of vitamin E on the oxidative stress develops due to antileprosy chemotherapy in leprosy patients was recorded (Srinivasan ***et al***. 2004; Das ***et al***. 2004; Vijayaraghavan ***et al***. 2005).

In the present study is carried out to evaluate the impact of vitamin E supplementation on the oxidative stress during BPA induced in albino rats blood (Jeff ***et al.*** 2002). The BPA induced rats kept for 20 days were fed with vitamin E (α-tocopherol) of 200mg/kg body wt. (Tang 1989; Bauersachs ***et al.*** 1993; Ibrahim ***et al***. 1997; Venkatraman ***et al***. 1998) for 15 days (Tang 1989; Shukla ***et al***. 1997; Manju ***et al***. 2005).

2. Literature Survey

Huang YF ***et al.*** (2017) investigate urinary NP and BPA levels in relation to biomarkers of oxidative /nitrative stress and inflammation and to explore whether changes in oxidative/ nitrative stress are a function of prenatal exposure to NP/BPA and inflammation in 241 mother-fetus pairs. The results support a role for exposure to NP and BPA and possibly inflammation in increasing oxidative/ nitrative stress and decreasing antioxidant activity during pregnancy

3. Materials and Methods

Animals
Male albino rats of Wistar strain weighing around 160 to 180gms were purchased from Tamilnadu Veterinary and Animal Sciences University, Chennai. The Animals were acclimatized to the laboratory conditions, fed with commercial pelleted rats chow (Hindustan Lever Ltd, Bangalore, India) and had free access to water. The experiments were designed and conducted in accordance with the guidelines of institutional animal ethics committee.

Experimental Protocol
The rats were divided into 4 groups comprising of 6 animals in each group.
Group I Control-sham operated animals (C)
Group II BPA induced (by oral) 20 days animals-Control (EC)
Group III BPA induced animals after 20 days given Vitamin E (ET vitE_{15})

The study was carried out to assess the oxidative stress, antioxidant enzymes, TSH, LDL and Protein in the BPA induced animal blood and under the influence of BPA induced and vitamin-E and tablet Thyronorm supplementation.

BPA induction
BPA was given to the albino rats by oral 20mg/ kg body weight for 20 days.

Vitamin E supplementation
Rats were fed with vitamin E (-tocopherol) of 200mg/Kg body weight, as reported earlier (*Tang, 1989; Bauersachs***et al.** 1993) for 15 days (*Manju**et al.**2005*).

Sample Preparation
The experimental animals were sacrificed by cervical dislocation at the end of the appropriate experimental period. The various experimental groups viz. C, EC, ET vitE, ETvitE_{15}&THY_{15} were dissected and heart punctured and blood sample were collected for analysis.

Oxidative damage assay
Oxidative damage in the muscle tissue was assessed by measuring the levels of TBARS in all the blood samples viz C, EC, ET vitE, ETvitE_{15}&THY_{15} were estimated according to the standard procedures described below.

TBARS (MDA)
TBARS (MDA) was measured in all the blood samples viz. C, EC, ET vitE, ET $vitE_{15}$&THY_{15} animals using the method of *Ohkawa* (1979).

Antioxidant enzyme assay
Super oxide dismutase, Catalase, Glutathione reductase enzymes were measured in all the blood samples viz. C, EC, ET vitE, ET$vitE_{15}$&THY_{15} animals according to the standard procedures described below.

Super oxide dismutase (EC. 1.151.1)
Super- oxide-dismutase enzyme was assayed in all the blood samples viz. C, EC, ET vitE, ET$vitE_{15}$&THY_{15}animals by using the method of Beauchamp and Fridovich (1974).

Super-oxide-dismutase (SOD) enzyme activity was expressed as Units / mg protein / min (one unit of SOD activity is defined as the enzyme reaction, which give 50% inhibition of NBT reduction in one minute under the assay condition).

Catalase (EC. 1.11.1.6)
Catalase was measured in all the blood samples viz. C, EC, ET vitE, ET$vitE_{15}$ &THY_{15}animals by using the method of Chance and Machly (1955).

Catalase (CAT) enzyme activity was expressed as µ moles of H_2O_2 consumed / min / mg protein.

Glutathione reductase: (EC. 1.6.4.2)

The activity level of glutathione reductase was measured in all the blood samples viz. C, EC, ET vitE, ET$vitE_{15}$ &THY_{15}animals by using the method of Racker, (1955).

Glutathione reductase (GR) enzyme activity was expressed as µ moles of NADPH oxidized/min/mg protein.

Statistical Analysis
The statistical analysis of the various parameters of the present study in all animal groups was carried out. Student't' test was conducted to test the difference between two sample means by using given formula as suggested by Gupta (1978)

4. Result and Discussion

The activity levels of thiobarbituric acid reactive substances was significantly elevated to 10% when compared to that of control (Table-2; Figure-2) The activity levels of antioxidant enzymes viz. super oxide dismutase (SOD), catalase (CAT), and glutathione reductase (GR) reduced to -14.28%, -13.51%, -12.63% respectively in the BPA induced albino rats when compared to that of control (Table -1; Figure -1)

TBARS was recorded a significant decrement 42.85% (Table-2; Figure2 -) indicating lowered lipid peroxidation in the BPA induced albino rat blood supplemented with vitamin E. The study on the antioxidant defense enzyme reveled a significant elevation of the activity levels of enzymes viz. SOD, CAT and GR in the blood samples of vitamin E fed BPA induced animals, the elevation of activity levels of enzymes ranges 37.5%, 62.5% and 71.08%.(Table-1; Figure-1a).

The oxidative stress leading to increased lipid peroxidation in the BPA induced albino rat was indicated by elevated levels of TBARS. Small amounts of malondialdehyde were produced during peroxidation and can react in the thiobarbituric acid test to generate a coloured product for photometric measurement. The measurement of level of TBARS which is the marker of oxidative stress induced lipid peroxidation reveal significant elevated levels in the BPA induced albino rats blood. Similar observations, where the free radicals generated lipid peroxidation were recorded in previous studies during BPA induction in albino rats blood sample.The increased levels of TBARS in the BPA induced rats blood sample indicating elevated lipid peroxidation which might be due to increased oxidative stress and/or decreased levels of antioxidant enzyme defense mechanism in the blood sample.

Further probe into the antioxidant defense mechanism of the BPA induced rats blood sample was carried out. The activity level of the cytosolic enzyme super-oxide-dismutase (SOD) recorded a significant decrease indicating decreased inhibition of formation of hydroxyl ion (·OH) from hydrogen peroxide, thereby increasing the free radical concentration leading to oxidative stress. The enzymes catalase (CAT) [Whose activity levels recorded depletion in the present study] prevent the formation of hydroxyl radicals that can initiate lipid peroxidation by converting the hydrogen peroxide into water and diatomic oxygen. The enzymatic antioxidant viz. superoxide dismutase (SOD), which catalyses the conversion of the oxygen radical (O_2·) to H_2O_2 (Somani ***et al***. 1996; Husain and Somani 1997, 1997a, b, c) and H_2O; the enzyme catalase (CAT) which then converts H_2O_2 to H_2O and oxygen (O_2); Further catalase (CAT) is involved in detoxification of high concentration of H_2O_2. The enzyme glutathione reductase (GR) catalyze the reaction to reconvert the GSSG to GSH. Hence working in concert, the peroxidase/reductase couple counter act oxidative stress in the blood.

The decreased levels CAT in BPA induced rats blood sample in the present study might suggest reduce detoxification of H_2O_2 and other peroxides which might lead to production of hydroxyl and peroxyl radical in the presence of iron (Gutteridge and Halliwell 1994; Rice-Evans and Burdon, 1994; Halliwell, 1996; Mares-Perlman ***et al***. 1996; Bast and Barr 1997). The depleted activity levels of glutathione reductase (GR) in the BPA induced rats blood sample, which is an important enzyme for the maintenance of intra cellular concentration of reduced glutathione (Chandra, 1992; Gutteridge and Halliwell 1994; Rice-Evans and Burdon, 1994; Diplock, 1995; Halliwell, 1996).

Thus the study on the oxidative stress and antioxidant enzyme defense system in BPA induced rats blood sample revealed an augmented oxidative stress due to BPA level in rat blood sample and decreased antioxidant enzyme defense which

might decrease the blood pumping efficiency and leading to the probable increase of oxidative stress in blood.

The increased lipid peroxidation in the BPA induced in ablbino rats blood might be due to increased generation of reactive oxygen species (ROS) in the muscle (Chapter I) thereby disturbing both enzymatic and non enzymatic antioxidant defense system in the blood. Vitamin E (α-tocopherol) serves as potent peroxyl radical scavenger. Excess generation of ROS may overwhelm natural antioxidant defenses such as serum vitamin E leading to lipid peroxidation in further contributing to serum damage (Ohyashiki ***et al.*** 1986; Bowles ***et al***. 1991; Meydani ***et al.*** 1993; Ohyashiki ***et al***. 1998).

The decrease levels of TBARS in the present study indicate the reduced lipid perocidation which might be due to the non enzymatic antioxidant vitamin E impact on the BPA induced in albino rats blood. Similar studies where vitamin E reduced lipid peroxidation were recorded (Ohyashiki ***et al.*** 1986; Bozkurt, 2002). The deranged antoxidant enzymatic defense system with the depleted activity levels of SOD, CAT and GR were significantly restored indicating the elevated activity levels of SOD, CAT and GR in the blood of BPA induced animals supplemented with vitamin E. This might be due to the free radicals scavenging act of vitamin E, thus reducing the free radical concentration and the probable regain of the antioxidant enzymatic defense system.

5. Conclusion

The above results envisage that the supplementation of vitamin E is an important lipid soluble antioxidant *invivo*, and it is presumed that its principle role is to protect membrane lipids from lipid peroxidation *invivo*, by scavenging lipid alkoxy or peroxy radicals which are capable of abstracting hydrogen from adjacent polyunsaturated lipid molecules to propagate a lipid peroxidation reaction and thus prevent the serum damage due to oxidative stress.

References

[1] Alonso-Magdalena P., Ropero A.B., Carrera M.P., Cederroth C.R., Baquié M., Gauthier B.R.,
[2] Nef S., Stefani E., Nadal A. Pancreatic insulin content regulation by the estrogen receptor ER alpha. PLoS One. 2008;3: 2069.
[3] Alonso-Magdalena P., Ropero A.B., Soriano S., Quesada I., Nadal A. Bisphenol-A: A new
[4] diabetogenic factor? Hormones. 2010;9: 118–126.
[5] Azzi A, Breyer I, Feher M, Ricciarelli R and Stocker A. Nonantioxidant functions of alpha-tocopherol in smooth muscle cells. J. Nutr. 2001; 131: 378S–81S.
[6] Azzi R. Engerbrtsen EM. French J and Jensen J. Glucose up take and metabolic stress in rat muscles stimulated electrically with different protocols. J.Appli.Physiol. 2000; 91:1237-1244
[7] Bast A and Barr PR. The antioxidant/prooxidant balance in neurodegeneration and
[8] neuroprotection. In: Bar PR. Beal MF. (Eds.). Neuroprotection in CNS Diseases. Marcel Deccer Inc.1997; 147-159
[9] Bauersachs S. Kirchgessner M and Paulicks BR. Effects of different levels of dietary selenium
[10] and vitamin E on the humoral immunity of rats. J Trace Elem Electrolytes Health Dis. 1993; 7:147-52.
[11] Bauersachs S. Kirchgessner M and Paulicks BR. Effects of different levels of dietary selenium and vitamin E on the humoral immunity of rats. J Trace Elem Electrolytes Health Dis. 1993; 7:147-52.
[12] Beauchamp and Fridovich. Isozymes of superoxide dismutase from wheat germ. Biochim Biophys Acta. 1974; 317:50-64.
[13] Bejma J and Ji LL. Aging and acute exercise enhance free radical generation in rat skeletal
[14] muscle.J Appl Physiol. 1999; 87(1):465-70.
[15] Bowles D, Torgan C, Ebner S, Kehrer J, Ivy J and Staines J. Effects of acute, submaximal exercise on skeletal muscle vitamin E. Free Radic Res Commun. 1991; 14:139–143.
[16] Bozkurt AK. α-tocopherol (vitamin E) and iloprost attenuate reperfusion injury in skeletal muscle in ischemia/reperfusion injury. J Cardio Surgery (Torino). 2002; 43: 693-696.
[17] Burton and Traber. 2+-initiated lipid peroxidation in phospholipid liposomes by a lipophilic aluminum complex, aluminum acetylacetonate. Biochem.Biophys Acta. 1990;1389(2): 141-149
[18] Calabrese V, Lodi R, Tonon C, D'Agata V, Sapienza M, Scapagnini G, Mangiameli A, Pennisi G, Stella AM and Butterfield DA. Oxidative stress, mitochondrial dysfunction and cellular stress response in Friedreich's ataxia. J Neurol Sci. 2005; 233(1-2):145-62.
[19] Calafat AM, Kuklenyik Z, Reidy JA, Caudill SP, Ekong J, Needham LL (2005) Urinary concentrations of bisphenol A and 4-nonylphenol in a human reference population.Environ Health Perspect 113:391–395
[20] Coors A, Jones PD, Giesy JP, Ratte HT (2003) Removal of estrogenic activity from municipal waste landfill leachate assessed with a bioassay based on reporter gene expression. Environ Sci Technol 37:3430–3434
[21] Chance B and Machly A.C Assay of Catalase and peroxidase. In: Colowick, S.P, (Ed.), Methods in enzymology. Academic Press, New York. 1955; 2: pp 764-775
[22] Chandra, R. Effect of vitamin and trace element supplementation in immune responses and infection in elderly subjects. Lancet, 1992; 340, 112- 1127.
[23] Diplock, A. Safety of antioxidant vitamins and beta-carotene. American J Clini Nutri. 1995; 62, 1510-1516.
[24] Gupta Sp. In: Statistical methods. (Ed) Gupta, Publ. Sultan Chand and Sons. New Delhi (1978)
[25] Gutteridge, J and Halliwell, B. Antioxidants in nutrition, health, and disease. 1994; 120- 124.

[26] Gutteridge, J and Halliwell, B. Antioxidants in nutrition, health, and disease. 1994; 120- 124.
[27] Harley KG, Aguilar Schall R, Chevrier J, Tyler K, Aguirre H, Bradman A, et. al. Prenatal and postnatal bisphenol A exposure and body mass index in childhood in the CHAMACOS cohort. Environ Health Perspect. 2013; 121; 514-20. Doi: 10.1289/ ehp. 1306866
[28] Halliwell B and Gutteridge JM. The importance of free radicals and catalytic metal ions in human diseases. Mol Aspects Med. 1985;8(2):89–193.
[29] Halliwell, B. Vitamin C: Antioxidant or Pro-oxidant in vivo? Free Radical Research,1996; 25, 439-454.
[30] Halliwell, B. Vitamin C: Antioxidant or Pro-oxidant in vivo? Free Radical Research,1996; 25, 439-454.
[31] Ibrahim W, Lee US, Yeh CC, Szabo J, Bruckner G and Chow CK. Oxidative stress and antioxidant status in mouse liver: effects of dietary lipid, vitamin E and iron.J Nutr. 1997;127(7):1401-6.
[32] Jeff SC, Benjamin RSL, Dodd H, Demirel A, Hisashi NR, Andrew S and Scott KP. Effects of vitamin E deficiency on fatigue and muscle contractile properties Eur J Appl Physiol 2002; 87: 272–277
[33] Ritter S (2011) Debating BPA's toxicity. Chem Eng News 89:5–13.
[34] Kim HT. Effect of the joint administration of selenium and vitamin E in combination with regular aerobic exercise on markers of lipid peroxidation and glutathione peroxidase in diabetic rats. Int J Sport Nutr Exerc Metab. 2005; 15(3): 266-278.
[35] Kim K., Park H. Association between urinary concentrations of bisphenol A and type 2 diabetes in Korean adults: A population-based cross-sectional study. Int. J. Hyg. Environ. Health. 2013;216:467–471. doi: 10.1016/j.ijheh.2012.07.007. [PubMed] [Cross Ref]
[36] Kim K[1], Son TG, Kim SJ, Kim HS, Kim TS, Han SY, Lee J. Suppressive effects of bisphenol A on the proliferation of neural progenitor cells. 2007 Aug; 70(15-16):1288-95.
[37] Lakind JS, Naiman DQ (2008) Daily intake of bisphenol A and potential sources of exposure: 2005–2006 National Health and Nutrition Examination Survey. J Expo Sci Environ Epidemiol 21:272–279
[38] Lim DS, Kwack SJ, Kim KB, Kim HS, Lee BM (2009) Potential risk of bisphenol A migration from polycarbonate containers after heating, boiling, and microwaving. J Toxicol Environ Health A 72:1285–1291
[39] Lee HC, Lim ML, Lu CY, Liu VW, Fahn HJ, Zhang C, Nagley P and Wei YH. Concurrent increase of oxidative DNA damage and lipid peroxidation together with mitochondrial DNA mutation in human lung tissues during aging--smoking enhances oxidative stress on the age tissues. Arch Biochem Biophys.1999; 362(2): 309-16.
[40] Kawagoshi Y, Fujita Y, Kishi I, Fukunaga I (2003) Estrogenic chemicals and estrogenic activity in leachate from municipal waste landfill determined by yeast two-hybrid assay. J Environ Monit 5:269–274.
[41] Lang IA, Galloway TS, Scarlett A, Henley WE, Depledge M, Wallace RB, Melzer D. Association of urinary bisphenol A concentrations with medical disorders and laboratory abnormalities in adults. JAMA. 2008; 300:1303-1310.doi; 10.1001/ Jama.300. 11. 1303.
[42] Lang IA, Galloway TS, Scarlett A. Association of urinary bisphenol a concentration with medical disorders and laboratory abnormalities in adults. J Am Med Assoc 2008;300:1303-10.
[43] Manju V. Balasubramaniyan V and Nalini N. Rat colonic lipid peroxidation and antioxidant status: the effects of dietary luteolin on 1,2-dimethylhydrazine challenge. Cell Mol Biol Lett. 2005; 10:535-51.
[44] Manju V. Balasubramaniyan V and Nalini N. Rat colonic lipid peroxidation and antioxidant status: the effects of dietary luteolin on 1,2-dimethylhydrazine challenge. Cell Mol Biol Lett. 2005; 10:535-51.
[45] Mares-Perlman, J. Klein, R. Klein, B. Greger, J. Brady, W. Palta, M. and Ritter, L. Association of zinc and antioxidant nutrients with age-related maculopathy. Arch. Ophthal. 1996; 114: 991-997.
[46] Meydani M. Evans WJ. Handelman G. Biddle L. Fielding RA. Meydani SN. Burill, J. Fiatarone MA. Blumberg JB and Cannon JG. Protective effect of vitamin E on exercise induced oxidative damage in young and older adults. Am. J Physiol 1993; 264:992–998;
[47] Ohkawa, H., Ohishi, N., and Kunio,Yagi. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal.Biochem 1979; 95, 351-358
[48] Ohyashiki T, Suzuki S, Satoh E, Uemori Y. A marked stimulation of Fe-initiated lipid peroxidation in phospholipid liposomes by a lipophilic aluminum complex, aluminum acetylacetonate. Biochem. Biophys Acta. 1998; 1389(2): 141-149.
[49] Ohyashiki T. Ushiro H. Mohri T. Effects of □ α- tocopherol on the lipid peroxidation and fluidity of porcine intestinal brush-border membranes. Biochem. Biophy. Acta. 1986; 858:294-300.
[50] Rice - Evans, C., Burdon, R. Free radical damage and its control. 1994; 14-19.
[51] Rubio-Gayosso I, Platts SH and Duling BR. Reactive oxygen species mediate modification of the glycocalyx during ischemia/reperfusion-injury. Am J Physiol Heart Circ Physiol. 2006 6 (online).
[52] Ropero, A. B., Alonso-Magdalena, P., Garc´ıa-Garc´ıa, E., Ripoll, C., Fuentes, E., and Nadal, A., (2008). Bisphenol-A disruption of the endocrine pancreas and blood glucose homeostasis.International Journal of Andrology, vol. 31, no. 2, pp. 194-199
[53] Shukla A, Rasik AM, Patnaik GK. Depletion of reduced glutathione, ascorbic acid, vitamin E and antioxidant defence enzymes in a healing cutaneous wound.Free Radic Res. 1997;26(2):93-101.
[54] Slater TF, Cheeseman KH, Davies MJ, Proudfoot K and Xin W. Free radical mechanisms in relation to tissue injury. Proc Nutr Soc. 1987 46: 1-12

[55] Somani SM, Husain K, Diaz-Phillips L, Lanzotti DJ and Kareti KR. Trammell GL. Interaction of exercise and ethanol on antioxidant enzymes in brain regions of the rat. Alcohol. 1996 ;13(6):603-10.
[56] Srinivasan S, Pragasam V, Jenita X, Kalaiselvi P, Muthu V and Varalakshmi P. Oxidative stress in urogenital tuberculosis patients: a predisposing factor for renal stone formation—amelioration by vitamin E supplementation.
Clin Chim Acta. 2004 ;350(1-2):57-63.
[57] Tang N. Appraisal of the protective effect of vitamin E against CCl_4 liver poisoning Zhonghua Yu Fang Yi Xue Za Zhi. 1989; 23:7-8.
[58] Tang N. Appraisal of the protective effect of vitamin E against CCl_4 liver poisoning Zhonghua Yu Fang Yi Xue Za Zhi. 1989; 23:7-8.
[59] Urano S. Yano K and Matsuo M. Membrane-stabilizing effect of vitamin E: Effect of α-tocopherol and its model compounds on fluidity of lecithin liposomes. Biochem. Biophys. Res. Comm. 1989; 150:469-475.
[60] Venkatraman JT, Angkeow P, Satsangi N and Fernandes G. Effects of dietary n-6 and n-3 lipids on antioxidant defense system in livers of exercised rats. J Am Coll Nutr. 1998 ;17(6):586-94.
[61] Vijayaraghavan R, Suribabu CS, Sekar B, Oommen PK, Kavithalakshmi SN, Madhusudhanan N and Panneerselvam C. Protective role of vitamin E on the oxidative stress in Hansen's disease(Leprosy) patients. Eur J Clin Nutr. 2005;59(10):1121-8.
[62] Xu JG, Tu YQ and Gu YD. Effect of electric stimulation on denervated skeletal muscle atrophy Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2003;17(5):396-9. Chinese.
[63] Zhang X, Chen, CH, Confino E, Barnes R, Milad M, Kazer RR. Increased endometrial thickness is associated with improved treatment outcome for selected patients undergoing in vitro fertilization embryo transfer. Fertility and Sterility. 2005; 83: 336– 340.

Table 1: Parameters of antioxidant enzymes in control and BPA & Vit E induced of male albino rats. Values are mean ±SD (n=10). Values with different letters are significantly different (P < O.OO1).

Parameter	Control (C)	% of changes	BPA Induced EC*	% of changes	BPA & Vit E Induced ET VitE15**
SOD Unit [1]/mg protein/min	0.56±0.8	-14.28	0.48±0.4	+37.5	0.66±0.7
CAT Unit [2] /mg protein/min	0.37±0.1	-13.51	0.32±0.1	+62.5	0.52±0.02
GR Unit [4] /mg protein/min	0.95±0.1	-12.63	0.83±.001	+71.08	0.24±.001

Unit [1] SOD = Superoxide dismutase activity, expressed as Units / mg protein / min (one unit of SOD activity is defined as the enzyme reaction, which give 50% inhibition of NBT reduction in one minute under the assay condition); **Unit [2] CAT** = Catalase activity, expressed as µ moles of H_2O_2 consumed / min / mg protein; **Unit [3]GR** = Glutathione reductase activity, expressed as µ moles of NADPH oxidized/min/mg protein;

*Group compared between control(C)and bpa induced (EC *)**Group compared between bpa induced (EC*) and bpa & vit E induced (ET vitE15) '¥' denotes statistical significance (P< 0.001)

Table 2: Parameters of oxidative damage in control and BPA & vitE induced of male albino rats. Values are mean ±SD (n=10). Values with different letters are significantly different (P < O.OO1).

Parameter	control (C)	% of changes	BPA induced EC*	% of Changes	BPA & Vit E Induced ET VitE15**
TBARS µ moles /mg protein	0.7±0.5	+10	0.63±0.05	-42.85	0.36±.001

TBARS = content in tissue, expressed as µ moles Malondialdehyde (MDA) /mg protein;
Group compared between control(C)and bpa induced (EC *)**Group compared between bpa induced (EC*) and bpa & vit E induced (ET vitE15) '¥' denotes statistical significance (P< 0.001)

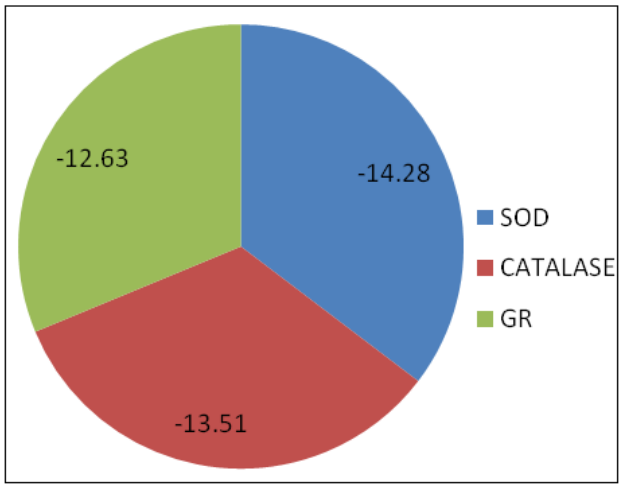

Figure 1 (a): Percentage change of activity levels of antioxidant enzyme viz. SOD, CAT and GR in control compared with BPA induced albino rats

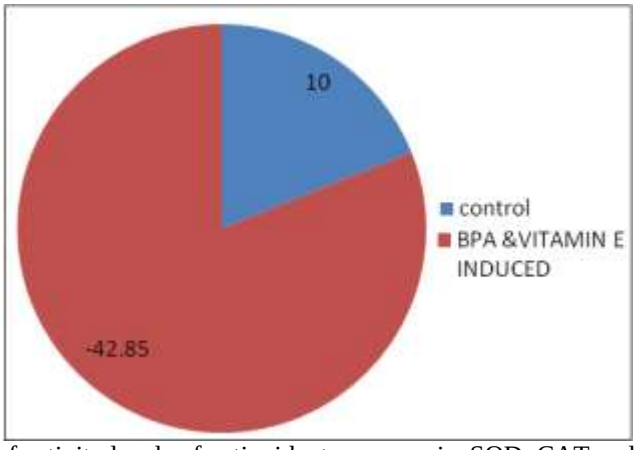

Figure 1 (b): Percentage change of activity levels of antioxidant enzyme viz. SOD, CAT and GR in BPA induced compared with Vitamin E supplemented albino rats

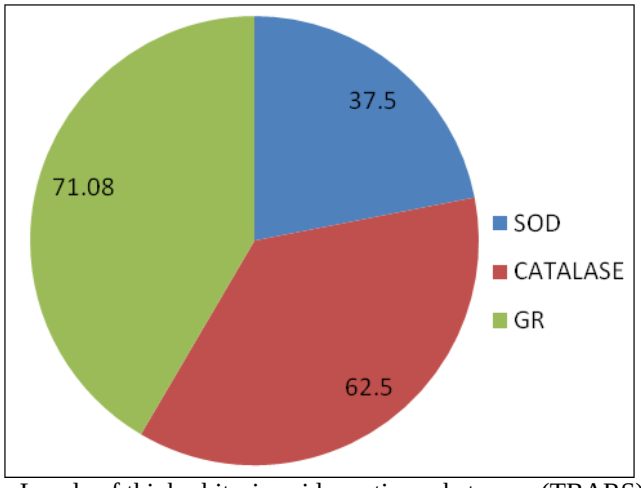

Figure 2: Percentage change in the Levels of thiobarbituric acid reactive substances (TBARS) in control and BPA &Vitamin E induced albino rats .