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Effect of *Lycopersicon esculentum* Mill (Tomato) Puree on the Liver Function and Oxidative Stress Biomarkers in Lead Acetate Exposed Wistar Rats

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ABSTRACT

Substantial quantity of lead escapes into the food chain leading to organ failure. This study investigated the effect of tomato puree on liver function and biomarkers of oxidative stress on lead acetate exposed rats. Twenty male albino rats were randomized into four groups of five rats. Normal control (NC) received water and feed only. Lead group (Pb) was given 50mg/Kg lead acetate. Standard control (Pb+Vit C) received 50mg/kg lead acetate + 100mg/kg vitamin C while the treatment group (Pb+TP) received 50mg/kg lead acetate + 400mg/kg tomato puree. Animals were allowed access to feed and water. Administration was done once daily by oral gavage for 28 days. Blood samples were analysed using standard procedures. One (1) Kg of tomato yielded 48.9% puree. Animals given 50mg/Kg lead acetate without treatment showed a significant ($p<0.05$) increases in the activities of Liver enzymes (AST, ALT and ALP) compared with the normal control. Administration of tomato puree and vitamin C improved the liver function parameters by decreasing significantly the elevated liver enzymes when compared with the untreated counterparts. The concentration of plasma albumin increased while bilirubin decreased significantly ($p<0.05$) in the same groups compared to the untreated. The catalase (CAT) and superoxide dismutase (SOD) activities were significantly ($p<0.05$) elevated while the concentration of malondialdehyde decreased significantly ($p<0.05$) in the treated groups compared with the untreated. These findings suggest that tomato puree can mitigate liver damage and oxidative stress caused by lead compounds and restore the normal function of both the liver and antioxidant system.

Keywords:
Lead,
tomato,
liver Function,
oxidative stress

INTRODUCTION

Lead is a heavy metal of public health concern and has been linked to a number of health challenges including multidimensional organ failure. A significant quantity of lead found in human system accumulates in the liver leading hepatic damage or injury (Ilesanmi et al., 2022). Lead being the most common environmental toxicant has received wide range of attention particularly on the mechanism of its toxicity.

One possible mechanism of lead toxicity to organs is by production of reactive oxygen species (ROS) which can lead to the induction oxidative stress resulting in the destruction of the organ membranes. The prevalence of lead as an environmental pollutant can be natural or anthropogenic. Anthropogenic activities such as combustion of coal and mineral oil, smelting, mining, processing of alloy and paint production by industries contribute significantly in raising the amount of lead in the environment.

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Vehicular emissions also contribute immensely to entry of lead into the food chain (Swarup et al., 2007). The unabated rise in the quantity of lead that enters the human and animal food chain has become a matter of global concern. Ironically, lead has no known beneficial biochemical, physiological or behavioural roles, rather investigators have documented detrimental roles of the lead as seen in peripheral and central nervous systems, animals haemopoietic systems, kidneys, liver cardiovascular and reproductive systems in both animals and human (Patra et al., 2007). The negative effect of lead involves setting an imbalance between generation and clearance of reactive oxygen species in the cell components such as cell membranes, DNA and cellular proteins. It has been reported that buildup of this excess ROS directly attacks the double bond of the fatty acid on cellular membranes causing a weakening effect on the adjacent C-H bonds which in turn makes oxidation easy through the removal of H-atom. The net effect of this oxidative process (also called lipid peroxidation) is loss of membrane function (Yiin and Lin, 1995). This also causes a consequential increase in the concentration of malondialdehyde (MDA) which serves as a marker of oxidative stress. Lead has also been suspected to be implicated in the alteration of antioxidant activities by directly inhibiting -SH groups in several antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx).

Tomato is one of the widely consumed fruit vegetables across various continents of the world. It is a component of commonly consumed dishes. Raw tomatoes are used in salads and processed one in juices, sauces, purees, concentrates and jams. In these diets they are valued for their taste, fragrance and health benefits. Reports have shown that tomato fruits play some beneficial roles in heart, brain and reproductive health. It has also been reported to have potential in reducing incidences of cancer, type 2 diabetes and constipation (Collins et al., 2022 The various health benefits of tomato fruits have been linked to its rich content in lycopenes. Lycopene is a phyto- compound belonging to carotenoid family which has been shown to possess antioxidant activities, protecting the body against damage due to free radicals.Lycopenes have been shown to contain eleven conjugated double bonds and consists of 40 carbon acyclic carotenoid. Its beneficial health effects include scavenging the singlet oxygen and active free radicals, modulation of intracellular communication, hormonal system, immune system, and metabolic pathways (Wieczorek, 2010). Research has shown that tomatoes are a good source of vitamin C, which is an antioxidant required for boosting of immunity and enhancing collagen synthesis (Collins et al.,2022). However, tomatoes grown in lead contaminated soil may possibly absorb lead from the soil leading to accumulation of the element in the fruits, thus consuming tomatoes grown in contaminated soil can pose a health risk as lead toxicity can have severe physiological effects (Oti et al., 2013). Therefore, it is crucial to ensure that the soil in which tomatoes are grown is free from lead or any other toxic metals to avoid any potential harm to human health.

In Ebonyi state, lead is mined in commercial quantities in Ndufu-Alike in Ikwo and Enyigba communities and there is the tendency of plants and animal inhabitants to be exposed to the harmful metal (Bello et al., 2019). Therefore, investigating the effects of lead on hepatic parameters and oxidative stress indices will provide practical insight to the possibility of using common fruits like tomato to mitigate environmental lead toxicity.

MATERIALS AND METHODS

SAMPLE COLLECTION

TOMATO FRUITS:

The tomato fruits used in this work was non-genetically modified species obtained from a local garden in Igbeagu community in Izzi L. G. A of Ebonyi State. The sample was authenticated by M. E. Nwankwo, a taxonomist with the department of applied biology, Ebonyi State University, Abakaliki. The sample was preserved in the University herbarum with voucher number EBSU-H-1007.

ALBINO RATS

A total of twenty (20) albino rates were procured from the pharmacology department of the University of Nigeria, Enugu Campus (UNEC), Enugu State.

EQUIPMENT, CHEMICALS AND REAGENTS:

All equipments used were optimally functional and chemicals/reagents were of high analytical quality.

PLATE 1. FRESH TOMATO FRUITS

PREPARATION OF TOMATO PUREE

One thousand grammes (1Kg) of fresh tomato were washed thoroughly with distilled water to remove unwanted entities like dust, dirt, pesticides and residues. The washed tomato fruits were drained on the rack, blanched at 95ºC for 5 minutes, peeled and the seeds separated out. After the seeds removal, the tomato was ground with blender. The resulting puree was weighed and the percentage yield calculated.

EXPERIMENTAL DESIGN

Twenty male albino rats weighing between 180 – 230g were randomly assigned into four groups of five rats. Group A was the normal control (NC) group and was given water and normal rat ration only for the 21 days that the experiment lasted. Group B served as the negative (Lead control – LC) and was given 50mg/Kg body weight of Lead acetate solution once daily for 3 weeks. Group C was the standard control (SC) group and was given 50mg/kg Lead acetate solution plus 100mg/kg vitamin C, while group D served as the treatment group (TG) and was given 50mg/kg body weight of lead acetate solution plus 400mg/kg tomato puree. All doses used of lead acetate, vitamin C and tomato puree were sub-lethal doses as determined by Obafemi *et al.* (2019). All administrations were through oral gavage and lasted for 21 days.

BLOOD SAMPLE COLLECTION

Blood samples were collected on the 21st day after 24 hours fasting and anaesthetization using diethyl ether. The blood sample collection was through ocular puncture into the lithium heparin bottles which was centrifuged at 2000g for five minutes and the resulting plasma isolated into plain bottles and refrigerated for liver function tests.

PREPARATION OF LIVER SAMPLE

The liver was harvested, homogenized in normal saline and centrifuged. Supernatant from the homogenate was refrigerated for use in the determination of oxidative stress indices.

BIOCHEMICAL ANALYSES

DETERMINATION OF LIVER FUNCTION PARAMETERS

The serum aspartate transaminase (AST) and alanine transaminase (ALT) activity was determined in accordance with the method of Reitman and Frankel (1957). The activity of alkaline phosphatase was determined following the method of Rec (1972). Serum albumin was determined in line with the method of Corcoran and Durnam (1977). Colorimetric method described by Jendrassik and Grof (1938) was used to estimate serum bilirubin.

DETERMINATION OF OXIDATIVE STRESS MARKERS

The activity of Superoxide Dismutase (SOD) was determined following the method of Kakkar *et al.* (1984). The method of Luck (1971) was used to determine catalase (CAT) activity in the liver homogenate while reduced plasma malondialdehyde (MDA) concentration was measured in line with the method of Wills (1966) as described by Ohkawa *et al*. (1979).

STATISTICAL ANALYSES

Data generated from the laboratory analyses were analysed using the statistical package for social sciences software (Version 25) and after which were subjected to one way analysis of variance (ANOVA). Values were expressed as mean ± standard error of the mean (SEM). P-values less than 0.05 were considered statistically significant. Data were finally subjected to Tukey Post Hoc comparison test.

RESULTS AND DISCUSSION

PERCENTAGE YIELD OF THE TOMATO PUREE

$$\% \text{ yield} = \frac{489}{1000} \times 100 = 48.9$$

Where 489 = weight of Puree after preparation, 1000 = Weight of Tomato fruits.

EFFECTS OF TOMATO PUREE ON LIVER FUNCTION OF LEAD EXPOSED ALBINO RATS

Result of the effects of tomato puree on the hepatic enzymes (AST, ALT and ALP) showed that exposure of the experimental animals to lead acetate caused a significant (P>0.05) rise in the activity of the enzymes as seen in the negative control (Lead control- LC) group with the peaks of the graph indicated as **'a'**. Treatment of the exposed animals with vitamin C and tomato puree recorded significant (P>0.05) decrease in the activities of AST, ALT and ALP when compared with the negative control group as indicated with graph peaks marked **c**, **c** and **b** and **b**, **b** and **b** respectively in Figure 1 . The AST and ALT in the tomato puree-treated group showed reduced serum activity of the liver enzymes similar with the group treated with vitamin C (standard control).

There was also observed significant (P>0.05) decrease in the plasma albumin concentration of the lead acetate exposed animals compared with the normal control (NC). However treatment of the animals with tomato puree and vitamin C caused a significant (P>0.05) increase in the serum concentration of the plasma protein – albumin as presented in Figure 2. The Lead-exposed animal group treated with tomato puree recorded a more significant (P>0.05) increase in the protein concentration compared with the vitamin C treated group (standard control)

The experiment showed that exposure of the animals to lead acetate resulted in a significant (P>0.05) increase in the concentration of serum bilirubin as presented in the Figure 3. While the Lead control (LC) group maintained a significantly high concentration of serum bilirubin, treatment of the experimental groups (TG) with vitamin C and tomato puree caused a significant(P>0.05) decrease in the serum concentration of bilirubin compared with the negative control (LC) group with the vitamin C treated group recording approximately same concentration as the normal control(NC) group.

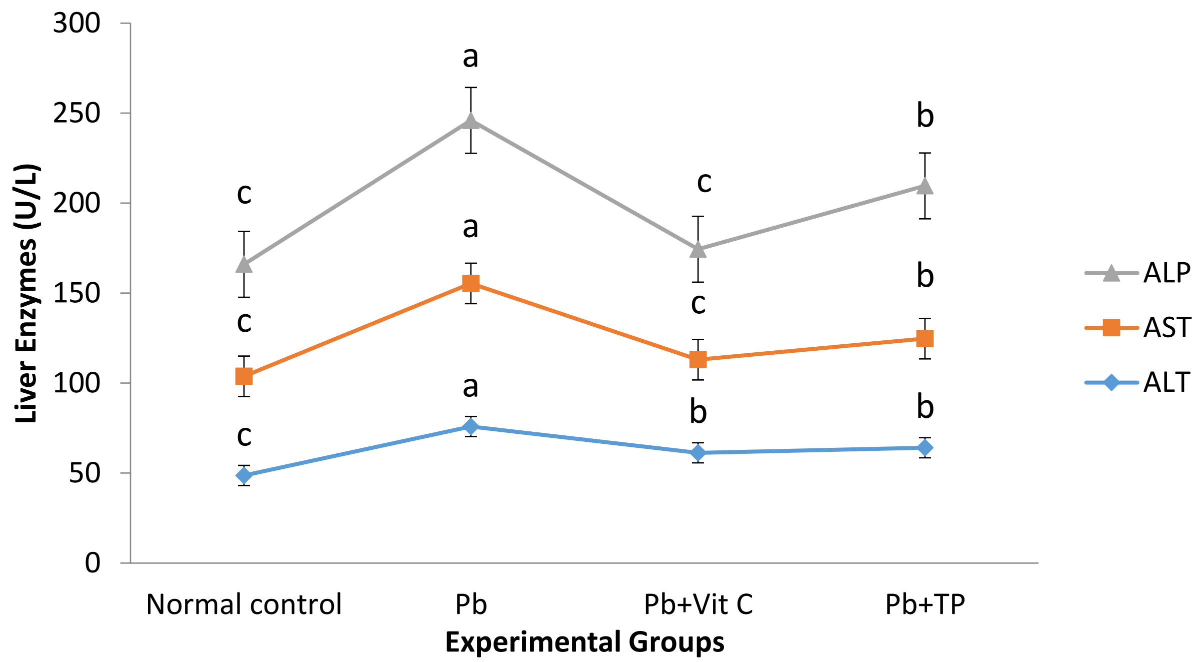

Figure 1: Liver Enzyme Activity of Lead Exposed Rats Treated with Tomato Puree Values are Expressed as Mean ± SEM (n=5). SEM: Bars with Different Alphabets are Significantly Different (P<0.05).

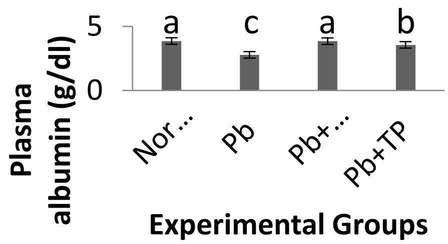

Figure 2: Plasma Albumin Concentration of Lead Exposed Rats Treated with Tomato Puree. Values are Expressed as Mean ± SEM (n=5). SEM: Bars with Different Alphabets are Significantly Different (P<0.05).

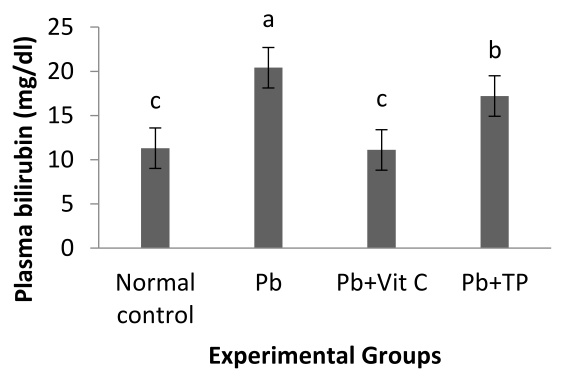

Figure 3: Plasma Bilirubin Concentration of Lead Exposed Rats Treated with Tomato Puree. Values are Expressed as mean ± SEM (n=5). SEM: Bars with

Different Alphabets are Significantly Different (P<0.05).

EFFECTS OF TOMATO PUREE ON BIOMARKERS OF OXIDATIVE STRESS ON LEAD EXPOSED ALBINO RATS.

Result of assay of catalase (CAT) activity in lead exposed rats showed that there was a significant (P>0.05) increase in the activity of the enzyme in the lead exposed groups compared with the normal control. Conversely, administration of vitamin C and tomato puree to the experimental groups resulted in a significant (P>0.05) decrease in the enzyme activity compared with the lead control group as shown in Figure 4. The figure shows that the tomato puree-treated (TP) group showed significant correlation in catalase activity with the standard control (SC) group.

A significant (P>0.05) higher activity of superoxide dismutase (SOD) activity was recorded in the Lead exposed group of the animals that received no treatment compared with the normal control (NC) group. However treatment groups that received vitamin C and tomato puree recorded significant (P>0.05) decrease in the activity of SOD compared with the negative control (LC) group. The result of SOD assay shows that the tomato puree exhibited comparable effect on the enzyme activity with the standard drug (Vitamin C).

Malondialdehyde (MDA) concentration was observed to be significantly (P>0.05) elevated in the animal group exposed to lead acetate compared with the normal control. However the consequent treatment with tomato puree and vitamin C resulted in a significant (P>0.05) reduction the concentration in plasma concentration of MDA compared with the lead control (LC) group. (Figure 6). The result also indicated that the tomato puree recorded quite significant (P>0.05) higher effectiveness in reducing the MDA concentration than the standard drug (vitamin C).

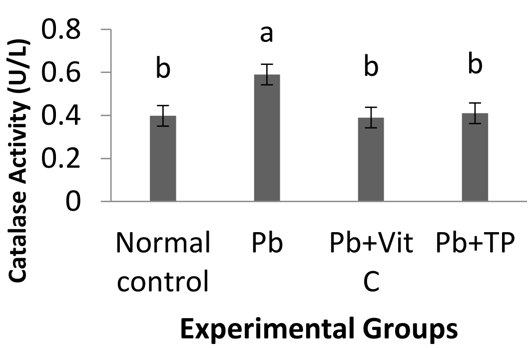

Figure 4: Catalase Activity of Lead Exposed Rats Treated with Tomato Puree. Values are Expressed as mean ± SEM (n=5). SEM: Bars with Different Alphabets are Significantly Different (P<0.05).

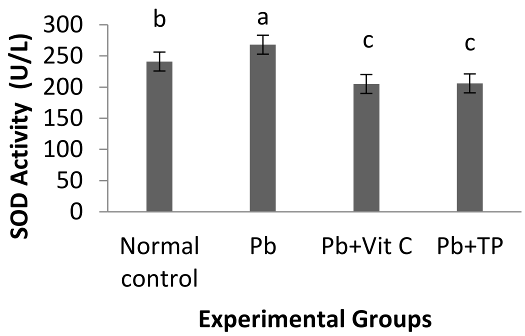

Figure 5: Superoxide Dismutase Activity of Lead Exposed Rats Treated with Tomato Puree. Values are Expressed as mean ± SEM (n=5). SEM: Bars with Different Alphabets are Significantly Different (P.05).

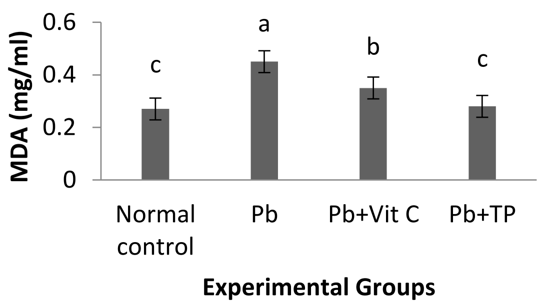

Figure 6: Malondialdehyde Conc. of Lead Exposed Rats Treated with Tomato Puree. Values are Expressed as mean ± SEM (n=5). SEM: Bars with Different Alphabets are Significantly (0.05) Different

Lead stands out as a heavy metal that has attracted the concerns of researchers due to its deleterious roles in the pathogenesis of several organ diseases. Entry and consequent accumulation of the metal has been linked to many organ failures. Lead has been associated with lipid peroxidation which is the primary cause of membrane damage leading to loss of membrane integrity (Samaila et al., 2025). As an environmental toxicant, lead has been reported to play a role in generating free radicals in the excess of the amount that the body can normally clear, thus setting an imbalance between free radicals production and clearance (Mititelu *et a*l., 2020). Naturally, the body produces compounds called antioxidants whose roles are to mitigate oxidation of molecules and protect the body against the damaging effects of free radicals produced due to cellular metabolism or as a result of environmental toxicants.

Similarly, antioxidants can be found in food especially fruits, vegetable and other diets derived from plants (Popović-Djordjević *et al*., 2022).

This study investigated the effects of tomato puree on liver and oxidative stress biomarkers in lead acetate exposed albino rats. The results showed that ingestion of Pb^{2+} induced a substantial stimulation of the activities of alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) in the plasma of the exposed animals. These liver enzymes are naturally membrane-bound and the observed increase in activity in the blood is a strong indication of possible damage to the hepatic tissue membranes causing leakage into the blood, a situation that might have been caused by exposure to lead acetate. It has been established that the two major biochemical functions of the liver are synthesis and excretion. The synthetic efficiency of the liver is estimated by serum levels of the proteins it produces such as albumin. Consequently, the plasma albumin concentration of the exposed albino rats in this work recorded a significant decrease, an observation that may be due to impaired synthesis in the liver signifying that the synthetic function of the liver might have been compromised as a result of exposure of the animals to lead acetate. Serum bilirubin was also observed to have been elevated in the animals exposed to lead acetate. Bilirubinn is a waste product of hemoglobin catabolism and it is usually excreted by the liver. In the face of impaired excretory function of the liver, bilirubin starts to build up in the blood, thus the observed increase in the concentration of plasma bilirubin in this work may not be unconnected with diminished excretory function of the liver as a result of exposure of the animals to lead acetate. The above results were in agreement with the work by Onyeneke and Omokaro (2016) who recorded elevated serum activities of ALT, AST, ALP and bilirubin with decreased serum albumin in occupationally exposed individuals in Benicity. These results are also consistent with findings previously reported (Nabil et al., 2012, Samuel et al., 2017, Azoz and Raafat 2012, Ibrahim et al., 2012 and Azab , 2014).

Conversely, administration of the exposed animals with tomato puree and vitamin C produced a substantial reversal effect in the activities of AST, ALT and ALP with concurrent elevation of plasma albumin and decreased plasma bilirubin. This observation can be attributed to the tomato puree possessing potential to repair the structural damage caused by exposure to lead acetate. The tomato puree's potential to reverse the indices of liver damage as potentiated by exposure to lead acetate may be linked to its rich content in lycopenes, vitamins C and A (Gurer-Orhan and Sabir, 2004) which might have acted synergically to restore the membrane integrity and reduce its permeability to the membrane bound liver enzymes. These findings are corroborated by previous works (Ibrahim et al.,2022, Hadayati et al., 2019 and Warenfo et al., 2011)

Oxidative stress plays crucial role in the general health and wellbeing of organisms, thus biomarkers of oxidative stress such as catalase, superoxide dismutase, glutathione reductase and malondialdehyde have been used in experiments to ascertain the potential health risk posed by exposure of an organism to certain toxicants in the environment (Konovalov et al., 2022; Painuli et al., 2022). The above enzymes called antioxidant enzymes play roles as scavengers of the singlet oxygen which is one of the most dangerous products of the oxidation reaction. The findings of the present study have revealed notable reduction in the plasma catalase (CAT) and superoxide dismutase (SOD) activities in the lead exposed rats. There was also observed concurrent and statistically significant increase in the plasma concentration of malondialdehyde (MDA) in the exposed animals. Hence, administration of tomato puree (TP) and vitamin C to the experimental groups resulted in substantial increase in CAT and SOD activities with consequent decrease in the plasma concentration of the malondialdehyde (MDA). This result is supported by Adelekan et al (2011) who previously observed a statistically significant increase in plasma catalase (CAT) activity in Lead exposed rats after supplementation with vitamin C and tomato puree. There is also a notable correlation of the findings of this research with that done by O'byrne (2002). The ability of tomato puree to reverse the unfavourable activities of the antioxidant enzymes may be due to the presence of certain phytocompound in tomato such as phenolics, lycopenes, flavonoids and several vitamins. Studies have provided evidence that these compounds possess antioxidant activities by mitigating the effects of free radicals (Stwart et al., 2000, Toor and Savage, 1992) . It can be suggested that these antioxidant compounds may have decreased the intracellular level of free radicals generated due to exposure to lead acetate either by inhibiting the activities or expression of the enzymes that enhance their production such as NADPH oxidase and xanthine oxidase or by enhancing the activities of superoxide dismutase, catalase or other enzymes with similar function of mopping up free radicals (Panchatcharam etal., 2006, Shih etal., 2007)

CONCLUSION

The findings in this work suggest that consumption of tomato puree can mitigate liver damage and oxidative stress caused by lead compounds and restore the normal function of both the liver and antioxidant system.

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