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Full Length Research Paper

Prevention of renal toxicity from lead exposure by oral administration of *Lycopersicon esculentum*

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For decades, lead (Pb) has being known for its adverse effects on various body organs and systems. In the present study, the ability of Pb to lower renal clearance (RC), as an index of renal function, was investigated and tomato (*Lycopersicon esculentum* : source of antioxidants) paste (TP) was administered orally to prevent the Pb's adverse effects. 54 Sprague Dawley rats, randomly divided into 3 groups (A, B and C) n = 18, were used for this study. Group A animals served as the control and were drinking distilled water. Group B and Group C animals were drinking 1% lead(II)acetate (LA). Group C Animals were, in addition to drinking LA, treated with 1.5 ml of TP/day. All treatments were for 8 weeks. Mann–Whitney U-test was used to analyse the results obtained. The results of this study showed that Pb caused a significant reduction in the weight gain, 24 h urine volume, RC, plasma and tissue superoxide dismutase (SOD) and catalase (CAT) activities, but a significant increase in plasma and tissue malondialdehyde (MDA) concentration. Administration of TP, however, prevented these Pb's adverse effects. These findings lead to the conclusion that oral administration of TP prevents Pb's adverse effects on the kidney mainly by preventing oxidation.

Key words: Renal clearance, tomato, lead, *Lycopersicon esculentum*, heavy metals, oxidative stress.

INTRODUCTION

Lead, a dangerous heavy metal, is harmful even in small amounts. Nevertheless, humans get exposed to Pb through their environment and diet (Gidlow, 2004). The manifestations of Pb poisoning in humans are nonspecific. They may include: loss of appetite, weight loss, anaemia (Khalil-Manesh et al., 1994; Waldron, 1966), sluggishness, memory loss (Hopkins, 1970), nephropathy, infertility (Patocka and Cerný, 2003) etc. However, oxidation accompanies lead toxicity (Hande et al, 2004), and its treatment include elimination of exposure, chelation therapy and often diet modification to ensure adequate essential metal (calcium and iron) intake (Markowitz, 2003).

Tomato, on the contrary, is a source of antioxidants (Lisa, 2002; Jeanie, 2007) and is made up by components (e.g. Lycopene, Glutation, Vitamin C, Vitamin A, Potassium and Calcium) very appropriate for detoxification, illnesses prevention (Nguyen and Schwartz, 1999), attaining growth (John and Marc, 2000), helping the immunologic system (Sandhu et al., 2000), maintaining blood in good state (Khalil-Manesh et al., 1994) etc. Lycopene has similar properties to the betacarotenes of the carrots and has anti-cancerous properties (John and Marc, 2000). Glutation has been shown to have antioxidant properties that help to eliminate free radicals. It is also very important in the elimination of the body toxins, especially heavy metals that produce deterioration of the organism by its accumulation. In addition glutation has the ability to lower blood pressure, favour the good state of our liver and prevent eczema (The world of plants, 2008). The vitamin A present in tomato helps the body to attain cellular growth (John and Marc, 2000), maintain the bones and the teeth in good state, help the immunologic system

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in combating infections (Sandhu et al., 2000) and to maintain sight in good state.

In addition the potassium and calcium components of tomato ensure availability of essential metals that are can compete with and displace lead, thus reducing its toxicity. These metals even play beneficial roles in bone formation, regulation of the corporal liquids, nerves, heart (Haddy et al., 2006) and the muscles (Ford and Podolski, 1970; Endo et al., 1970). It has also been documented that oral administration of tomatoes may increase blood parameters such as Haematocrit, RBC, WBC etc (Khalil-Manesh et al., 1994).

Furthermore, the detoxifying components and the health-protective antioxidants of tomato are more available for absorption and more potent in cooked tomato than in raw uncooked one (Gärtner et al., 1997; John and Marc, 2000; Thompson et al., 2006).

This research, therefore, centres on whether oral administration of cooked tomatoes prevents Pb induced renal toxicity or not, using renal clearance and tissue oxidation as major indicators.

MATERIALS AND METHODS

54 adult male Sprague Dawley rats (180 - 220 g) were used for this study. They were inbred at the animal house section of the department of physiology, Ladoke Akintola university of technology, Ogbomoso. The animals were acclimatized over a period of 2 weeks.

Preparation of tomato paste (TP)

TP was prepared by grinding tomatoes and heating it in water a bath for 45 min at 80^{O}C.

Grouping of animals and treatment

The rats were randomly grouped into three (A, B and C), n = 18. Animals in group A served as the control group and were drinking distilled water. Animals in group B and group C were drinking 1% lead (II) acetate (LA) (Marchlewicz et al., 1993). Group C animals were, in addition to drinking LA, treated with 1.5 ml of TP/day. All treatments were for 8 weeks.

Animal sacrifice and collection of samples

24 h after the last treatment, each animal was transferred to metabolic cage equipped with accessory for collecting urine. The 24 h urine sample was collected and its volume recorded for each animal. Each rat was weighed, then and sacrificed by cervical dislocation. Blood samples were collected by cardiac puncture. Blood collected from each rat was divided into 2: one half in plain bottle and the other half in EDTA bottle. Plasma and serum were obtained from blood samples by spinning at 3000 rpm for 20 min.

Collection of data and statistical analysis

Each kidney was homogenized. Kidney homoginate was used in determining kidney SOD activity, kidney CAT activity and kidney MDA concentration. The Weight Increase and 24- hour Urine volume (ml) were recorded. To obtain creatinine and urea clearance, urine and serum creatinine concentration were determined using Alkaline Picrate Method described by Jaffe (1886); urine and serum Urea concentration were determined using Diacetylmonoxime Method described by Ceriotti and Spandro (1963). Renal clearance was then calculated using the formula "Clearance of Y = (Urine concentration of Y * 24hr Urine volume) /Plasma concentration of Y" as documented by Guyton and Hall (2001). Plasma and tissue superoxide dismutase (SOD) activity were determined using the method described by Fridovich (1986). Plasma and tissue catalase (CAT) activity were determined using the method described by Sinha (1972). Plasma and Tissue Malondialdehyde (MDA) Concentrations were determined using the procedure described by Varshney and Kale (1990).

The data obtained are presented as mean ± SD. The "Control Group" and the "Test Groups" were compared using the Mann–Whitney U-test. The significance level was set to a P-value < 0.05.

RESULTS

The following results were obtained and are presented as mean ± SEM. Level of significance is taken at "P value < 0.05" (*) and/or "P value < 0.01" (**).

Weight increase (g)

Comparing their final and initial weight showed that there was significant weight gain (P value < 0.05) is in all the groups over the 8 weeks of the research. There was, however, no significant difference (P value > 0.05) in weight gain of group C and control, while group B had a significantly smaller weight gain.

Kidney weight (g)

The kidney weight of group B was significantly lower (P value < 0.05) than that of the control, while there was no significant difference in the kidney weight of group C and that of the control.

24 h urine volume (24 HrUV) (ml)

The 24 HrUV for group B was significantly (p value < 0.05) lower than that of the control (Group A). While 24 HrUV of group C D showed no significant difference (P value > 0.05) from that of the control.

Creatinine clearance

A significant (p value < 0.05) decrease was noticed in the renal creatinine clearance of group B when compared to control; while group C showed no significant (p value > 0.05) difference from the control.

Urea clearance

Group B had renal urea clearance (RUC) that is signifi-

Table 1. Weight increase across the three groups during the 8 weeks of research.

	Group A	Group B	Group C
Weight before sacrifice (g)	219.3 ± 0.987	198.9 ± 0.543	218.5 ± 0.324
Initial weight (g)	183.2 ± 1.021	182.1 ± 0.342	184.5 ± 0.443
Weight increase (g)	36.1 ± 0.334	16.8 ± 0.987*	34.0 ± 0.943
P value (when compared with control)		0.0439	0.1163

* "P value < 0.05"

Table 2. Comparison of kidney weight across the groups.

	Group A	Group B	Group C
Kidney weight (g)	0.6028 ± 0.055	0.5235 ± 0.033*	0.6421 ± 0.057
P value (when compared with control)		0.03064	0.2269

cantly (p value < 0.05) lower than that of the control. While RUC of group C was not significantly (p value > 0.05) lover than that of the control.

Plasma superoxide dismutase (SOD) activity

Group B showed a highly significant (P value < 0.01) decrease in plasma SOD activity. Group C was, however, not significantly (P value > 0.05) different from the control in terms of plasma SOD activity.

Plasma catalase (CAT) activity

Group B showed a highly significant (P value < 0.01) decrease in plasma CAT activity. However, group C showed no significant (P value > 0.05) difference in CAT activity from the control.

Plasma malondialdehyde (MDA) concentration

Group B showed significant (P value < 0.05) increase in plasma MDA concentration; while group B showed no significant (P value > 0.05) difference from control.

Tissue superoxide dismutase (SOD) activity

Group B showed a highly significant (p value < 0.01) decrease in plasma SOD activity, there was, however, no significant (p value > 0.05) difference between the Tissue SOD Activity of Group C and that of the Control.

Tissue catalase (CAT) activity

Group B, showed a significant (p value < 0.05) decrease in tissue CAT activity. However, group C showed no significant (p value > 0.05) difference from control.

Tissue malondialdehyde (MDA) concentration

Group B showed a significant (p value < 0.01) increase in tissue MDA concentration. While MDA concentration in group C was found to be significantly lower when compared with group C.

DISCUSSION

The results of this study shows that exposure to Pb for 8 weeks significantly (p value < 0.05) reduces weight gain (Table 1), this is in support of the findings of Suzan et al. (1999) and can be linked to the less efficient metabolic processes associated with Pb toxicity (Struzy ska et al., 1997). Administration of 1.5 ml TP/day, however, annuls this Pb's adverse effect on weight gain. This may be partly due to the fatty acid composition of TP (Cantarelli et al., 1993) and more importantly due to presence of health-protective antioxidants such as lycopene, vitamin C and vitamin A in TP (Jeanie, 2007) despite its relatively low caloric value (21 Kcal/100 g) and low protein content (0.85% by weight) (The world of plants, 2008). These can also explain the significant (p value < 0.05) decrease in kidney weight (Table 2) noticed in animals exposed to Pb (Group B) and the no significant (p value > 0.05) decrease in kidney weight noticed in animals administered TP alongside Pb exposure (Group C) since organ weights are normally fractions of the body weight (within specific range).

There was no significant (p value > 0.05) decrease in the 24 HrUV (Table 3) of animals treated with TP even though they were as well exposed to Pb. On the contrary, the lead only group (Group B) showed significant (p value < 0.05) reduction in 24 HrUV. This is because Pb (like most other heavy metals) interferes with glomerular filtration rate (GFR) and tubular processes, tubular reabsorption and/or tubular secretion, (Oberley et al., 1995; Machiko et al., 1978) which are the major determinants of urine volume. The administered tomato would therefore be responsible for the prevention of these lowering effects of Pb on 24 HrUV by preventing the lowering of GFR.

Table 3. Comparison of 24 HrUV (ml) across the groups.

	Group A	Group B	Group C
24 HrUV (ml)	3.12 ± 0.112	2.30 ± 0.108*	2.94 ± 0.068
P value (when compared with control)		0.0139	0.1298

* "p value < 0.05"

Table 4. Comparison of creatinine clearance across the 3 groups

	Group A	Group B	Group C
Creatinine clearance	3.455 ± 0.121	2.831 ± 0.148*	3.303 ± 0.097
P value (when compared with control)		0.0341	0.2291

* "p value < 0.05"

Table 5. Comparison of urea clearance across the 3 groups.

	Group A	Group B	Group C
Urea clearance	0.3718 ± 0.062	0.2578 ± 0.042*	0.3209 ± 0.094
P value (when compared with control)		0.0222	0.3252

* "p value < 0.05"

Table 6. Plasma SOD activity across the Groups

	Group A	Group B	Group C
Plasma SOD activity	1.766 ± 0.052	1.123 ± 0.061**	1.701 ± 0.092
P value (when compared with control)		0.0098	0.4113

** "P value < 0.01"

In a similar way renal creatinine clearance (RCC) and renal urea clearance (RUC) of animals treated with tomato alongside Pb were not significantly different (p value > 0.05) from those of the control (Table 4 and Table 5 respectively). Meanwhile, animals treated with Pb only showed significant (p value < 0.05) decrease in RCC and RUC. This supports the findings of Machiko et al. (1978) which say that heavy metal toxicity brings about reduction in renal clearance among other renal dysfunctions. But TP significantly (p value < 0.05) reduced the Pb's adverse effects on RC, such that there was no significant difference in RC of control and that of Pb + TP group.

There was no significant (p value > 0.05) difference in SOD activity of both the plasma and tissue (Tables 6 and 9 respectively) of the control and that of the animals treated with tomato alongside Pb. On the contrary, there was a highly significant (p value < 0.01) decrease in plasma and tissue SOD activity in animals treated with Pb only compared to the control. This finding is in agreement with Ping-Chi and Yueliang (2002) and is at the same time in support of *Lycopersicon esculentum* (tomato) as an antioxidant.

Furthermore, there was a significant decrease in both plasma CAT Activity (p value < 0.01) and tissue CAT Activity (p value < 0.05) of animals treated with Pb only relative to control (Tables 7 and 10 respectively). There was, however no significant (p value > 0.05) difference between the control and the animals treated with tomato alongside Pb in this respect. This further establishes that it was TP that reduced the oxidative stress that Pb could cause.

These significant decreases in the activities of both plasma and tissue SOD and CAT activity, resulting from Pb exposure, would have markedly reduced the level of anti-oxidation defenses in the body. This is in support of the fact that oxidation through free radical (e.g. Reactive Oxygen Species, ROS) accompanies Pb toxicity (Hande et al, 2004).

Finally, there was no significant (p value > 0.05) difference in both plasma and tissue MDA concentration (Tables 8 and 11 respectively) of control and those of the animals treated with tomato alongside Pb. While animals treated with Pb only showed a significant increase in both plasma (p value < 0.05) and tissue (p value < 0.01) MDA concentration. This confirms that it was TP, source of antioxidants (Lisa, 2002; Jeanie, 2007), that reduced the

Table 7. Plasma CAT activity across the groups.

	Group A	Group B	Group C
Plasma CAT activity	0.4101 ± 0.082	0.2173 ± 0.032**	0.3997 ± 0.095
P value (when compared with control)		0.0093	0.5192

** "P value < 0.01"

Table 8. Plasma MDA concentration across the groups.

	Group A	Group B	Group C
Plasma MDA concentration (µg/g protein)	1400.3 ± 23.01	1813.6 ± 11.18*	1419.5 ± 22.07
P value (when compared with control)		0.0424	0.5370

* "P value < 0.05"

Table 9. Tissue SOD activity across the groups.

	Group A	Group B	Group C
Tissue SOD activity	1.534 ± 0.076	1.203 ± 0.074**	1.497 ± 0.085
P value (when compared with control)		0.0092	0.3646

** "p value < 0.01"

Table 10. Tissue CAT activity across the groups.

	Group A	Group B	Group C
Tissue CAT activity	0.3357 ± 0.052	0.2256 ± 0.056*	0.3739 ± 0.046
P value (when compared with control)		0.0214	0.1754

* "p value < 0.05"

Table 11. Tissue MDA concentration across the 3 groups.

	Group A	Group B	Group C
Tissue MDA concentration(µg/g protein)	1367.9 ± 1.94	1954.1 ± 3.79**	1305.1 ± 2.76
P value (when compared with control)		0.0069	0.2633

** "p value < 0.01"

oxidative stress that Pb exposure could have caused in the animals.

It can, thus, be concluded that exposure to Pb lowers renal clearance due to Pb's ability to cause oxidative stress by interfering with the activities of SOD and that of CAT and thereby given freedom to free radicals (e.g. ROS) to cause oxidation which manifests as increase in the concentration of MDA (in the case of lipid peroxidation). Oral administration of *L. esculentum* (in the form of tomato paste, TP), however, prevented these Pb induced reduction in renal clearance. This would be mainly due to the anti-oxidant characteristics of the constituents (e.g. lycopene) of *L. esculentum* (administered as TP).

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