



# Influence of *Polyalthia longifolia* (Sonn) leaves on oxidative stress biomarkers in the kidney of cadmium-induced toxicity rats

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## Abstract

*Polyalthia longifolia* (Sonn.) (False ashoka) is well-known in traditional system of medicine for its medicinal and therapeutic uses. However, the ameliorative effect of this plant against cadmium-induced oxidative stress in rat model has not been reported. Hence, this preliminary study investigates the prophylactic and the curative effects of aqueous and methanolic leaf extracts of *Polyalthia longifolia* against cadmium-induced nephrotoxicity in rats. Animals in group I served as control and administered distilled water only; group II was administered cadmium (4 mg/kg/body weight) every other day for 14 days; rats of groups III and IV served as the prophylactic group and were pre-treated with *P. longifolia* aqueous and methanolic leaf extract for 7 days and then exposed to cadmium for 7 days; and groups V, VI, VII, and VIII served as curative groups and were firstly exposed to cadmium for 7 days and then post-treated with 100 mg and 200 mg/kg body weight of aqueous extract and 100 mg and 200 mg/kg body weight of methanolic extract *P. longifolia* for another 7 days. Cd intoxication significantly ( $p < 0.05$ ) increased the activities of serum creatinine and C-reactive protein levels. Cd exposure caused a significant increase ( $p < 0.05$ ) in tissue total cholesterol and triglyceride levels. The levels of renal antioxidant parameters: glutathione-s-transferase, superoxide dismutase, catalase, glutathione reductase, and reduced glutathione, were significantly ( $p < 0.05$ ) decreased in Cd-intoxicated rats with concomitant elevation of lipid peroxidation. Histopathological examination confirms the biochemical findings. Pre- and post-treatment with *P. longifolia* restored antioxidant status, improved lipid profiles, and attenuated the lesions in the tissues. Both extracts of *P. longifolia* protects against Cd-induced kidney toxicities via antioxidant activities.

**Keywords** *Polyalthia longifolia* · Cadmium · Nephrotoxicity · Oxidative stress · Antioxidant · Histopathology

## Introduction

Cadmium (Cd) toxicity remains a major public health burden due to its global pervasiveness and its devastating effects on the renal system because the metal can enter the food chain, thereafter undergoes bioaccumulation and thus endangering human health (Roccheri et al. 2004; Flora et al. 2006). Cd is toxic, has a long biological half-life, and is a non-biodegradable metal that is non-beneficial to plants, animals, and humans (Jarup et al., 2000). The prolonged environmental and occupational exposure may contribute to the dysfunctions of the renal,

hepatic, hematological, and reproductive systems in man and animals (Flora et al. 2006; El-Sayed and El-Neweshy, 2009).

A principal mechanism of Cd toxicity is lipid peroxidation despite its inability to directly generate free radicals under physiological conditions (Eneman et al. 2000). The toxicity effect of Cd has been investigated in many organs: it is reported that Cd can induce tissue damage via oxidative damage to cellular organelles by the induction of reactive oxygen species (ROS) generation (Stohs et al. 2000; Cuypers et al. 2010) and change the expression of DNA at the epigenetic level (Luparello et al., 2011; Wang et al., 2012). Also, the inhibition or upregulation of transport pathways of the kidney tubules notably at the proximal S1 segment in particular (Thévenod, 2010; Vesey, 2010) has also been documented to also initiate Cd toxicity. Other mechanisms include heme synthesis inhibition (Schauder et al. 2010), interactions with bioelements (Bulat et al. 2012; Bulat et al. 2017), and impairment of mitochondrial function leading to apoptosis and cancer (Wallace et al. 2019). Glutathione depletion has been observed, which has a distortion in the architectural framework of proteins due to the binding of Cd to sulfhydryl groups (Valko

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et al. 2005). Central to the abovementioned mechanisms of Cd toxicity in the organs is the generation of free radicals and/or ROS. Consequent upon this, the use of antioxidant therapy should be an essential part in the treatment of Cd poisoning. There is an increasing interest towards the use of naturally occurring phytochemicals with nephroprotective and antioxidant activity in Cd intoxication therapy.

Medicinal plants have played an invaluable role in the drug discovery process as a result of an avalanche of bioactive natural compounds called secondary metabolites accumulated in various plant organs and specialized cells (Ekor, 2013). These secondary metabolites have biological activities present in plant extracts and their constituents such as polyphenols, flavonoids, and essential oils that have a beneficial effect on health and function as natural antioxidants (Adesanoye et al. 2016; Molehin et al. 2018). Among these medicinal plants is *Polyalthia longifolia* (Sonn.) with reported therapeutic activities.

*Polyalthia longifolia* (Sonn.) (False ashoka) (family, Annonaceae) is a tall evergreen tree vastly distributed throughout the country of Africa, South and South Eastern Asia, Australia, and New Zealand. In folklore medicine, *Polyalthia longifolia* (*P. longifolia*) has been used for the treatment of several diseases such as fever, skin diseases, and hypertension (Kirtikar and Basu, 1995). Some of the most important identified and/or isolated antioxidant compound derivatives from *Polyalthia longifolia* plant are 16-hydroxycyclohexa-3,13(14)E-dien-15-oic acid (Katkar et al. 2010) or quercetin, quercetin-3-O- $\beta$ -glucopyranoside, kaempferol-3-O- $\alpha$ -rhamnopyranosyl-(1  $\rightarrow$  6)- $\beta$ -galactopyranoside, kaempferol-3-O- $\alpha$ -rhamnopyranosyl-(1  $\rightarrow$  6)- $\beta$ -glucopyranoside, rutin, and allantoin (Sashidhara et al. 2011), which are reported in literature to confer several health benefits from this plant. Some of the documented pharmacological activity of *P. longifolia* includes antiulcer activities (Malairajan et al. 2008), hepatoprotective anti-inflammatory (Tanna et al. 2009) activities, hypoglycemic and antihyperglycemic (Nair et al. 2007) activities, and antimicrobial (Faizi et al. 2003; Murthy et al. 2005; Nair and Chanda, 2006) activities. However, to the best of our knowledge, no study has been carried out on the protective role of *P. longifolia* in cadmium-induced oxidative stress and toxicity in rats. Therefore, this study was designed to evaluate the ameliorative effect of *Polyalthia longifolia* leaf against cadmium-induced nephrotoxicity in rats.

## Materials and methods

### Plant sample collection

The leaves of *P. longifolia* were collected between November and December 2017 in Ekiti State University, Ado-Ekiti, Nigeria. It was identified and authenticated at the

Department of Plant Science and Biotechnology, Ekiti State University Ado-Ekiti, Nigeria, and a sample has been deposited at the University herbarium with voucher specimen number (UHAE-2018/102).

### Reagents and chemicals

Cadmium sulfate, trichloroacetic acid (TCA), 1-chloro-2,4-dinitrobenzene (CDNB), thiobarbituric acid (TBA), 5',5'-dithiobis(2-nitrobenzoic acid) (DTNB), hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), and reduced glutathione were procured from Sigma-Aldrich Co. (St. Louis, MO, USA). Total cholesterol (TC), triglycerides (TRIG), total protein (TP), creatinine diagnostic kits, and rat C-reactive protein (CRP) ELISA kits were purchased from BD Biosciences Ltd. (San Diego, CA, USA). All other chemicals used in this experiment were of analytical grade.

### Plant extraction

Two different extraction methods from leaves were used in this study to obtain aqueous (AEPL) or methanolic (MEPL) extracts. *P. longifolia* leaves were washed and air-dried for 7 days. The dried leaves were blended using an electric grinder. The powdered leaves obtained were then extracted by dissolving 500 g in 1000 ml of distilled water for 72 h for the aqueous extract (AEPL). The resultant mixture obtained undergoes a process of filtration and the filtrate obtained was freeze-dried. This freeze-dried extract was later reconstituted in distilled water and stored in a fridge prior to analysis. For the methanolic extract, 500 g of the powdered leaves was dissolved with 1000 ml of methanol for 72 h as described by the method of Farooq (2009) and evaporated to yield the crude extract. The combined methanol extract was filtered and then concentrated by rotary evaporator to obtain the crude extract.

### Experimental animals

Healthy adult male Wistar rats weighing between 180 and 200 g were purchased from the College of Medicine, Ekiti State University, Ado-Ekiti, Nigeria. The rats were placed under natural conditions (12-h light/12-h dark) each day, and they ate standard pellets and had free access to water. In this study, all the animals used were handled gently in accordance with established guidelines written in the Guide for the Care and the Use of Laboratory Animals. The animal experiments were carried out in line with our institutional supervision of the ethics committee and standards on animal care of our Institution.

## Experimental design

Thirty-two (32) male Wistar rats were randomly divided into eight (8) groups of four (4) rats each. Animals in group I served as a normal control for both prophylactic and curative studies and received orally distilled water for 14 days. Group II served as a toxic control for both prophylactic and curative studies and received cadmium (4 mg/kg/body weight) every other day for 14 days as described by Ojo et al. (2014). Groups III and IV served as the pre-treatment groups (prophylactic) and received aqueous and methanolic extract of *P. longifolia* at a dose of 100 mg/kg orally for 7 days, respectively, and were exposed to cadmium (4 mg/kg/body weight) for another 7 days. Groups V, VI, VII, and VIII served as the post-treatment groups (curative). They were exposed firstly to cadmium (4 mg/kg/body weight) for 7 days and later treated with aqueous extract of *P. longifolia* at a dose of 100 mg/kg (group V) and 200 mg/kg (group VI), likewise for the methanolic extract of *P. longifolia* at a dose of 100 mg/kg (group VII) and 200 mg/kg (group VIII) for another 7 days, respectively. The rats were administered these *P. longifolia* leaf extract doses and Cd doses during this study based on previous trial studies carried out in our laboratory and by also following the modified methods of Ojo et al. (2014) and Orororo et al. (2018). Animals were fasted overnight and sacrificed 24 h after the last treatment via cervical dislocation.

## Blood and tissue homogenate preparation

Blood sample was obtained via cardiac puncture into plain centrifuge tubes and was left to stand for 1 h. Preparation of the serum was done by centrifuging at 3000×g for 15 min in a Beckman bench centrifuge. The supernatant obtained was used for the determination of serum biochemical parameters. The kidney was quickly dissected, excised, and rinsed in 1.15% KCl, thereafter blotted with the aid of filter paper and weighed. After which, it was placed in an ice-cold phosphate buffer (pH 7.4) and thereafter homogenized. The kidney homogenates were centrifuged at 12,000×g for 15 min at 4 °C to obtain post mitochondrial fractions (PMF) which was kept at 4 °C and used for further biochemical assays.

## Experimental protocol

### Biochemical assays

Creatinine, total cholesterol (TC), and triglyceride (TG) levels were measured in the serum by spectrophotometric methods using Randox commercial assay kits following the manufacturer's protocol while rats' CRP levels were estimated in the separated serum using the rat CRP ELISA kit purchased from BD Biosciences Ltd. (San Diego, USA), following the manufacturer's protocol.

## Biomarkers of oxidative damage

Lipid peroxidation was determined by assessing the thiobarbituric acid reactive substances (TBARS) formed (expressed as MDA equivalents) as described by Ohkawa et al. (1979). The level of malondialdehyde (MDA) was deduced from the absorbance as described by Adam-Vizi and Seregi (1982) and the unit stated as nmol MDA/mg protein. The reduced GSH determination was carried out according to the method of Jollow et al. (1974).

## The antioxidant enzyme activities

The activity of superoxide dismutase (SOD) was evaluated as outlined by the method of Misra and Fridovich (1972). The activity of catalase (CAT) was assessed as described by Asru (1972). The glutathione peroxidase (GPx) activity was estimated as described by Lawrence and Burk (1961). Glutathione reductase (GR) was investigated using the method of Elliott et al. (1992). The protein content determination was carried out as described by the method of Lowry et al. (1951) using bovine serum albumin (BSA) as standard.

## Histological assessment

The kidney samples were already in 10% formalin and were paraffin-embedded. Fine cut sections were taken and stained with hematoxylin and eosin (H&E) for microscopic examinations (Disbrey and Rack, 1970) by a histopathologist who was blinded to the study design.

## Data analysis

The data collected was analyzed using one way analysis of variance (ANOVA) and expressed as mean ± standard deviation (SD) which was followed by Duncan's multiple range test. The value of  $p < 0.05$  was considered significant. The level of significance was set at  $p < 0.05$ .

## Results

### Effects of *Polyalthia longifolia* on biochemical indices and lipid profile of Cd-exposed rats

Cd exposure caused a significant ( $p < 0.05$ ) increase in the levels of serum total protein, creatinine, and CRP (Table 1). Pre-treatment and post-treatment with *Polyalthia longifolia* significantly ( $p < 0.05$ ) ameliorated Cd-induced increase in total protein, creatinine, and C-reactive protein levels. In Table 2, Cd intoxication significantly ( $p < 0.05$ ) increased the levels of renal total cholesterol and triglyceride respectively. Administration of *Polyalthia longifolia* both at

**Table 1** Effect of aqueous and methanolic extracts of *Polyalthia longifolia* on creatinine, C-reactive protein (CRP), and total protein in the serum of rats intoxicated with cadmium sulfate

Group	Treatment	Protein (g/dl)	Creatinine (mg/dl)	CRP (mg/dl)
Group I	Normal	23.8 ± 0.43	0.17 ± 0.04	3.17 ± 0.07
Group II	Cd (4 mg/kg oral)	8.64 ± 0.48*	0.78 ± 0.15*	5.17 ± 0.07*
Group III	AEPL 100 mg/kg + Cd (prophylactic)	18.48 ± 0.34**	0.20 ± 0.08**	3.84 ± 0.16**
Group IV	MEPL 100 mg/kg + Cd (prophylactic)	22.86 ± 0.09**	0.23 ± 0.21**	2.25 ± 0.21**
Group V	Cd + AEPL 100 mg/kg (curative)	21.24 ± 0.04**	0.18 ± 0.38**	2.08 ± 0.51**
Group VI	Cd + AEPL 200 mg/kg (curative)	22.59 ± 0.19**	0.19 ± 0.04**	2.50 ± 0.03**
Group VII	Cd + MEPL 100 mg/kg (curative)	21.24 ± 0.04**	0.18 ± 0.38**	2.08 ± 0.51**
Group VIII	Cd + MEPL 200 mg/kg (curative)	17.38 ± 0.34**	0.17 ± 0.22**	2.50 ± 0.03**

Values are expressed as mean ± SD ( $n = 4$ ). AEPL, aqueous extract of *Polyalthia longifolia*; MEPL, methanolic extract of *Polyalthia longifolia*; Cd, cadmium

\*Significantly different from control ( $p < 0.05$ )

\*\*Significantly different from Cd ( $p < 0.05$ )

prophylactic and curative dose ( $p < 0.05$ ) attenuated the elevated levels of these lipid indices to near normal in the tissues of Cd-exposed rats.

### Effects of *Polyalthia longifolia* on antioxidant parameters of tissues of Cd-exposed rats

Cd intoxication significantly increased ( $p < 0.05$ ) renal lipid peroxidation products measured as thiobarbituric acid reacting substances (expressed as MDA equivalents) (Table 2). However, treatment with *P. longifolia* almost completely ameliorated Cd-induced increase in MDA. In Cd-exposed rats, the activities of renal SOD, CAT, and levels of GSH decreased significantly ( $p < 0.05$ ) when compared with those of controls (Table 3). In addition, the activities of renal GPx, GST, and GR decreased significantly ( $p < 0.05$ ) in Cd-exposed rats when compared with those in controls (Table 3). Pre- and post-treatment with aqueous and methanolic extract of *P. longifolia* reversed the adverse effect of Cd by normalizing these antioxidant indices in rats.

**Table 2** Changes in the levels of lipid peroxidation and lipid profile in cadmium-induced rats

Group	Treatment	MDA ( $\mu\text{mol/mg}$ protein)	TC (mg/dl)	TRG (mg/dl)
Group I	Normal	0.96 ± 0.33	0.33 ± 0.07	21.87 ± 0.36
Group II	Cd (4 mg/kg oral)	2.06 ± 0.37*	0.58 ± 0.01*	39.71 ± 0.20*
Group III	AEPL 100 mg/kg + Cd (prophylactic)	1.25 ± 0.05**	0.49 ± 0.03**	28.34 ± 0.06**
Group IV	MEPL 100 mg/kg + Cd (prophylactic)	1.88 ± 0.11	0.40 ± 0.06**	29.43 ± 0.10**
Group V	Cd + AEPL 100 mg/kg (curative)	1.71 ± 0.02**	0.48 ± 0.06**	28.00 ± 0.22**
Group VI	Cd + AEPL 200 mg/kg (curative)	1.14 ± 0.04**	0.44 ± 0.03**	25.99 ± 0.02**
Group VII	Cd + MEPL 100 mg/kg (curative)	1.93 ± 0.13	0.43 ± 0.03**	25.03 ± 0.14**
Group VIII	Cd + MEPL 200 mg/kg (curative)	1.03 ± 0.22**	0.38 ± 0.03**	23.99 ± 0.22**v

Values are expressed as mean ± SD ( $n = 4$ ). MDA, malondialdehyde; AEPL, aqueous extract of *Polyalthia longifolia*; MEPL, methanolic extract of *Polyalthia longifolia*; Cd, cadmium; TC, total cholesterol; TRG, triglycerides

\*Significantly different from control ( $p < 0.05$ )

\*\*Significantly different from Cd ( $p < 0.05$ )

### Effects of *Polyalthia longifolia* on histology of tissues of Cd-exposed rats

Figure 1 reveals that Cd intoxication caused severe necrosis and distortion of cytoarchitecture of renal tissue while administration with aqueous and methanolic extract of *P. longifolia* preserved the morphology and number of glomeruli and also restored the architectural layout of the renal tissue.

### Discussion

Cadmium is recognized as one of the most toxic pollutants in the environment and it is a known human carcinogen (Liu et al. 2013). The chronic intake of Cd in contaminated foods or air results in organ dysfunctions via cell death, resulting in pulmonary, hepatic, and renal tubular diseases (Salinska et al. 2013). In this study, the modulatory effects of *P. longifolia* against Cd-induced kidney toxicities and oxidative stress were

**Table 3** Changes in the levels of kidney antioxidant parameters in cadmium-induced nephrotoxicity rats treated with aqueous and methanolic extracts of *Polyalthia longifolia*

Group	Treatment	GSH (mg/g protein)	GPx (mmol H <sub>2</sub> O <sub>2</sub> consumed/min/mg protein)	GR (mg/g tissue)	SOD (U/mg protein)	CAT (U/mg protein)
Group I	Normal	0.075 ± 0.028	143.8 ± 0.749	37.79 ± 0.65	0.203 ± 0.141	0.089 ± 0.009
Group II	Cd (4 mg/kg oral)	0.014 ± 0.028*	107.3 ± 0.770*	13.79 ± 0.74*	0.066 ± 0.084*	0.022 ± 0.010*
Group III	AEPL 100 mg/kg + Cd (prophylactic)	0.011 ± 0.077**	124.4 ± 0.113**	36.02 ± 0.83**	0.103 ± 0.028**	0.036 ± 0.003**
Group IV	MEPL 100 mg/kg + Cd (prophylactic)	0.021 ± 0.014**	128.9 ± 0.721**	19.45 ± 0.15**	0.082 ± 0.028**	0.038 ± 0.013**
Group V	Cd + AEPL 100 mg/kg (curative)	0.046 ± 0.014**	136.1 ± 0.714**	32.45 ± 1.38**	0.081 ± 0.084**	0.030 ± 0.005**
Group VI	Cd + AEPL 200 mg/kg (curative)	0.058 ± 0.014**	138.7 ± 0.007**	34.09 ± 0.62**	0.090 ± 0.056**	0.054 ± 0.002**
Group VII	Cd + MEPL 100 mg/kg (curative)	0.035 ± 0.021**	125.1 ± 0.707**	21.85 ± 0.84**	0.103 ± 0.028**	0.060 ± 0.005**
Group VIII	Cd + MEPL 200 mg/kg (curative)	0.039 ± 0.021**	134.9 ± 0.823**	24.3 ± 0.08**	0.115 ± 0.056**	0.062 ± 0.010**

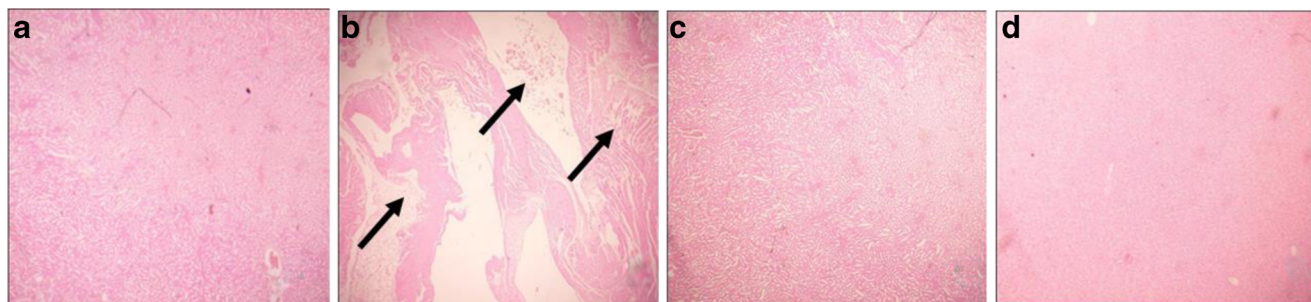
Values are expressed as mean ± SD ( $n = 4$ ). CAT, catalase; GPx, glutathione peroxidase; GSH, reduced glutathione; SOD, superoxide dismutase; GR, glutathione reductase; AEPL, aqueous extract of *Polyalthia longifolia*; MEPL, methanolic extract of *Polyalthia longifolia*; Cd, cadmium

\*Significantly different from control ( $p < 0.05$ ). \*\*Significantly different from Cd ( $p < 0.05$ )

investigated in rats. Our findings revealed that both pre-treatment and post-treatment with *P. longifolia* extracts could impede Cd-induced kidney oxidative stress and dyslipidemia in the rats. It has been reported in the literature that Cd can initiate peroxidation of membrane polyunsaturated fatty acids by overproducing free radicals accompanied by intracellular antioxidant defense armory inhibition (Roopha and Padmalatha 2004; Prabu et al. 2013). In agreement with these findings, a significant elevation in renal lipid peroxidation levels in Cd-exposed rats and a sharp decline in the activities of antioxidant enzymes were observed in this study (Tables 2 and 3). In addition to ROS induction, Cd toxicity may induce the expression of certain stress genes which may significantly affect the activities of some antioxidant enzymes (Wang et al. 2013; Martínez-Paz et al. 2014).

Cd-induced nephrotoxicity in rats was assessed by determining the levels of serum creatinine and CRP. C-reactive protein levels are a marker of inflammation and are synthesized mainly in the liver and regulated by circulating interleukin (Pasceri et al. 2000). Emerging evidence suggests that elevated plasma levels of CRP have become one of the

strongest independent predictors of kidney diseases (Ridker et al., 1998; David et al. 2005). This study showed a significant ( $p < 0.05$ ) increase in creatinine and CRP levels in cadmium-induced group when compared with the normal control group (Table 1). This observation could be a result of destruction caused by cadmium in cellular membrane components, especially of the proximal tubular cells which lead to tubular dysfunction. Damage to kidney cells as a result of Cd has been reported by El-Maraghy et al. (2001) and Kara et al. (2005). The present study is in agreement with this previous report in that creatinine and CRP levels were significantly increased in Cd-exposed rats. Interestingly, pre- and post-treatment with aqueous and methanolic extract of *P. longifolia* significantly reduced Cd-induced kidney dysfunction by decreasing the levels of creatinine and CRP in Cd-exposed rats to near normal values when compared with those in the control (Table 1). This might imply that *P. longifolia* leaves have a protective effects against cadmium-induced nephrotoxicity. These findings are also similar to the work reported by Adaramoye and Akanni (2016).



**Fig. 1** Histopathological changes in rat's kidney caused by cadmium and the protective effect of *P. longifolia* in different groups. Kidney section ( $\times 400$ ) of rat treated with normal saline without visible lesions (**a**); cadmium (4 mg/kg body weight) showing a severe necrosis and distortion of

cytoarchitecture of renal tissue (**b**); cadmium + 200 mg/kg body weight of *P. longifolia* (curative dose) aqueous extract showing no visible lesions (**c**); and cadmium + 200 mg/kg body weight of *P. longifolia* (curative dose) methanolic extract showing no visible lesions (**d**)

Furthermore, it has also been reported that lipoprotein abnormalities which arise from the disruption of serum and cellular lipid levels account for the commencement of Cd-mediated dyslipidemia (Jurczuk et al. 2004). Additionally, exposure to Cd may cause an alteration to lipid metabolism and contribute to the progression of tissue-associated disorders. In this study, we observed a significant increase in the levels of renal total cholesterol and triglyceride in Cd-exposed rats when compared with those in their corresponding control groups. The results are in agreement with the findings of Navaneethan and Rasool (2014). The changes in the total cholesterol and triglyceride profiles as seen in Cd-treated rats may be explained by the ability of this metal to increase the activity of 3-hydroxy-3-methylglutaryl CoA reductase (Kayama et al. 1995). Administration of *P. longifolia* leaf extracts significantly normalized the upregulated lipids and lipoprotein levels in tissues of the Cd-exposed animals through anti-lipoperoxidative and antioxidant actions, which inhibit the extensive accumulation of cholesterol and oxidized lipid components as well as prevention of hypercholesterolemia. The protective effect of *P. longifolia* against Cd intoxication confirmed by biochemical indices was also corroborated by histological findings.

In this study, the renal SOD and CAT activities were significantly decreased in Cd-exposed rats. The result is consistent with the findings of Navaneethan and Rasool (2014) and Prabu et al. (2013) that Cd exposure elevates lipid peroxidation and causes antioxidant enzyme inhibition, resulting in oxidative damage to the heart, kidney, and testes. SOD is a well-known diagnostic index for determining the free radical reactions involving oxygen. It performs its defensive role against oxidative tissue damage through the dismutation superoxide radicals. Furthermore, the elevated MDA levels in Cd-induced rats may be a result of significant decrease in the SOD activities (Samuel et al. 2011). The current study shows that Cd-exposed rats had significantly reduced the activities of GPx, GST, GR, and GSH with respect to control groups. GPx is involved in the catalyzed reaction of reduced glutathione to oxidized glutathione by the action of hydroperoxides (Halliwell and Gutteridge 1999) while GST, a group of enzymes, is involved in detoxification of xenobiotics such as drugs and carcinogens, and hence protect the cells against oxidative stress (Matés 2000). In addition, GSH a non-enzymatic antioxidant serves as a cofactor for GST. The observed decline in the activities of these antioxidant indices in the renal tissues of Cd-exposed rats is similar to the report of Navaneethan and Rasool (2014). A reasonable explanation for the reduction in these antioxidant enzyme activities is the fact that accumulation of Cd in tissues increases the consumption of glutathione (Onyema et al., 2006) and the drop in GSH causes the inactivation of the other antioxidant enzymes. Likewise, It has been documented too that the binding of Cd directly to the sulfhydryl (SH) groups in the active sites of

these enzymes with the corresponding metal cofactors' displacement from the active sites may lead to these enzyme inhibitions (Renuga-devi and Prabu 2009). Pre-and post-treatment with aqueous and methanolic extract of *P. longifolia* significantly increased the activities of antioxidant enzymes and decreased the MDA levels in the kidney of Cd-intoxicated rats, probably due to the free radical scavenging role of *P. longifolia* and presence of some bioactive components in the plant. In addition, the pre- and post-treated group exhibited modulatory effect in reducing the toxicity both in the treated group before and after exposure to cadmium. These findings support the reported study that *P. longifolia* leaf extract is a rich source of phenolic compounds and other effective antioxidants (Katkar et al. 2010; Sashidhara et al. 2011) when administered prior to cadmium exposure (pre-treated) or after exposure to cadmium (post-treated) and causes significant improvement of toxicity in the kidney of rats.

In conclusion, our study reveals that aqueous and methanol extract of *P. longifolia* could protect renal tissues of rats from Cd-induced oxidative stress and dyslipidemia. The exact mechanism of the protection offered by this plant extract may involve the scavenging of free radicals generated during Cd metabolism in vivo and/or induction of antioxidative enzymes. Further studies are required to elucidate detailed molecular mechanism of action of this plant extract against Cd-induced toxicity.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All institutional and national standards for the care and use of laboratory animals were followed. This article does not contain any studies with human participants performed by any of the authors.

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