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ORIGINAL ARTICLE

Ameliorative effect of *Parinari curatellifolia* seed extracts on sodium nitroprusside–induced cardiovascular toxicity in rats

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Abstract

The pharmacological potential of *Parinari curatellifolia* has remained largely unexplored by the scientific community and little information is available to support the folkloric and ethnobotanical uses of the plant. This present study was carried out to investigate the ameliorative effect of *P. curatellifolia* seed extracts on sodium nitroprusside (SNP) toxicity on the heart and artery in rats. *P. curatellifolia* seed crude aqueous-methanolic extract (CMPC) as well as n-hexane (HFPC), dichloromethane (DFPC), ethyl acetate (EFPC), and n-butanolic (BFPC) fractions was prepared and screened for phytoconstituents. In the in vitro test, crude extract and fractions were assessed for antiperoxidative potential in SNP-induced lipid peroxidation (LPO) in rat heart and artery. For in vivo assessment, CMPC (400, 500, and 600 mg/kg bwt) and the fractions (5 and 6 mg/kg bwt) were co-administered with 5 mg/kg SNP to Wistar rats for 7 days. Extent of LPO in the heart and artery and serum activities of aspartate transaminase (AST) and alanine transaminase (ALT) as well as concentrations of bilirubin, creatinine, urea, and uric acid were evaluated. The result of phytochemical screening revealed the presence of alkaloids, tannins, saponins, flavonoids, terpenoids, phlobatannins, and cardiac glycosides. SNP toxicity significantly ($p < 0.05$) increased LPO, bilirubin, creatinine, urea, and uric acid levels as well as the activities of AST and ALT. However, the extracts reversed the effect of SNP toxicity. The study revealed the protective effect of *P. curatellifolia* against SNP-induced cardiovascular toxicity in rats. The study plant could serve as a good therapeutic agent to combat cardiovascular-related complications.

Keywords Cardioprotection · Lipid peroxidation · *Parinari curatellifolia* · Phytochemical · Sodium nitroprusside

Introduction

Plants have a long history of use and of claimed health benefits. However, herbal supplements and botanicals have potent pharmacological activity and, consequently, contribute to potential adverse effects and drug interactions (Bernardini et al. 2018). Many bioactive chemotherapeutic and prophylactic agents have been isolated from plants and some of these have been used as templates for the synthesis of many pharmacological important compounds (Cseke et al. 2016). *Parinari curatellifolia* Planch. Ex Benth., is an evergreen tropical tree of Africa, the common name of which is Mobola plum, belongs to the family Chrysobalanaceae. It is called Abere and Rura in Yoruba and Hausa, respectively, while the leaf, stem, and bark are used in Nigeria as an alternative medicine for the treatment of pile, diabetes, nervous disorder, skin infections, cough, and as antipyretic and anti-helminthic remedies either alone or in combination with other herbs (Ogbonnia et al. 2011). Some of its pharmacological uses include its hypolipidemic and hypoglycemic activities (Manuwa et al. 2017; Crown et al. 2017a), anti-diabetic and cardioprotective (Ogbonnia et al. 2011), antihypertensive (Crown et al. 2017b), and hepatoprotective (Olaleye et al. 2014) potentials. The pharmacological potential of the plant has remained largely unexplored by the scientific community and little information is available to support the folkloric and ethnobotanical uses of the plant.

Sodium nitroprusside (SNP, Na_2 [Fe $(CN)_5NO]\cdot 2H_2O$) is a potent pro-oxidant that could potentiate oxidative stress and tissue damage via its release of cyanide and/or nitric oxide

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Table 1 Phytochemical constituents in crude aqueous-methanolic extract and solvent fractions of *Parinari curatellifolia* seed

Phytoconstituents	Crude/solvent fractions				
	CMPC	HFPC	DFPC	EFPC	BFPC
Alkaloids	+	−	+	−	+
Saponins	+	−	−	−	+
Tannins	+	−	−	−	+
Flavonoids	+	−	−	+	−
Terpenoids	+	+	−	−	−
Phlobatannin	+	−	−	−	−
Anthraquinone	−	−	−	−	−
Cardiac glycosides	+	+	+	−	+
Steroidal rings	+	+	−	−	−
Deoxy sugar	+	−	−	−	+
Cardenolides	+	−	+	−	+

CMPC crude aqueous-methanolic extract of *Parinari curatellifolia* seed, *HFPC* n-hexane fraction from CMPC, *DFPC* dichloromethane fraction from CMPC, *EFPC* ethyl acetate fraction from CMPC, *BFPC* n-butanol fractions from CMPC. + (positive), present; − (negative), absent

(NO) (Grossi and D'Angelo 2005). Although, NO is very crucial to the functioning of the vascular system, due to its ability to vasodilate endothelia tissue, including both arterioles and venules (venules more than arterioles), hence, maintains vascular tension/relaxation (Al-Imam and Sulaiman 2012). However, researchers make use of SNP to simulate the excess production of NO in the situation of increased reactive oxygen species (ROS) production caused by the release of cyanide (Posser et al. 2006; Hottinger et al. 2014; Duvenage et al. 2019; Rolly et al. 2019). Excess NO reacts with ROS, such as singlet oxygen/superoxide produced under oxidative stress, and form peroxynitrite (ONOO–), which, at physiological pH, protonates to form peroxynitrous acid (HOONO), a relatively long-lived oxidant (Posser et al. 2006) and a potent species, capable of causing endothelial and neuronal damages (Ayala et al. 2014), as well as vascular rigidity (Vallurupalli and Mehta 2017). Despite this toxic effect, the SNP is still in use in certain clinical circumstances such as malignant hypertension or for rapid control of blood pressure during vascular surgery and neurosurgery. Interestingly, the use of natural products rich in antioxidant that can scavenge ROS such as ONOO– has been reported in the management of vascular diseases such as hypertension (Al Disi et al. 2016; Oboh et al. 2018). This study is carefully designed to investigate the ameliorative effects of *P. curatellifolia* seed extracts on SNP toxicity.

Materials and methods

Chemicals

Sodium nitroprusside was purchased from Sigma-Aldrich, Saint Louis, MO, USA. Sigma Chem. Co. (London, UK). Alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, creatinine, urea, and uric acid kits were obtained from Randox Laboratories, UK. All other chemicals were of analytical grade. All other chemicals used for this research were of good quality and analytical grade. Kenxin (Model KX3400C) model of refrigerated centrifuge and JENWAY UV-visible spectrophotometer (Model 6305;

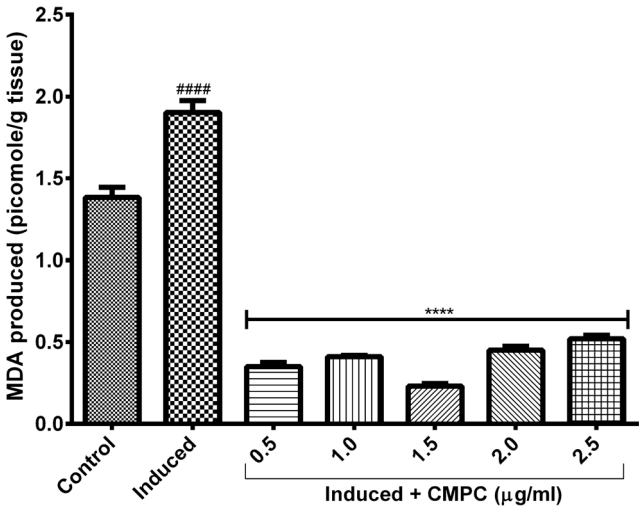

Fig. 1 Effect of crude aqueous-methanolic extract of *Parinari curatellifolia* seed on sodium nitroprusside–induced lipid peroxidation in the artery of albino rats in vitro. Results are expressed as mean ± SD ($n = 3$). $^{\#\#\#\#}p < 0.0001$ vs control, $^{****}p < 0.0001$ vs induced. CMPC, crude methanolic extract of *Parinari curatellifolia* seed; MDA, malonyldialdehyde

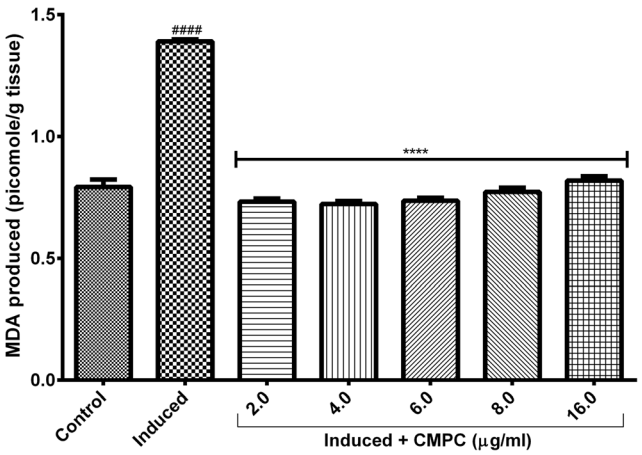

Fig. 2 Effect of crude aqueous-methanolic extract of *Parinari curatellifolia* seed on sodium nitroprusside–induced lipid peroxidation in the heart of albino rats in vitro. Results are expressed as mean ± SD ($n = 3$). $^{\#\#\#\#}p < 0.0001$ vs control, $^{****}p < 0.0001$ vs induced. CMPC, crude methanolic extract of *Parinari curatellifolia* seed; MDA, malonyldialdehyde

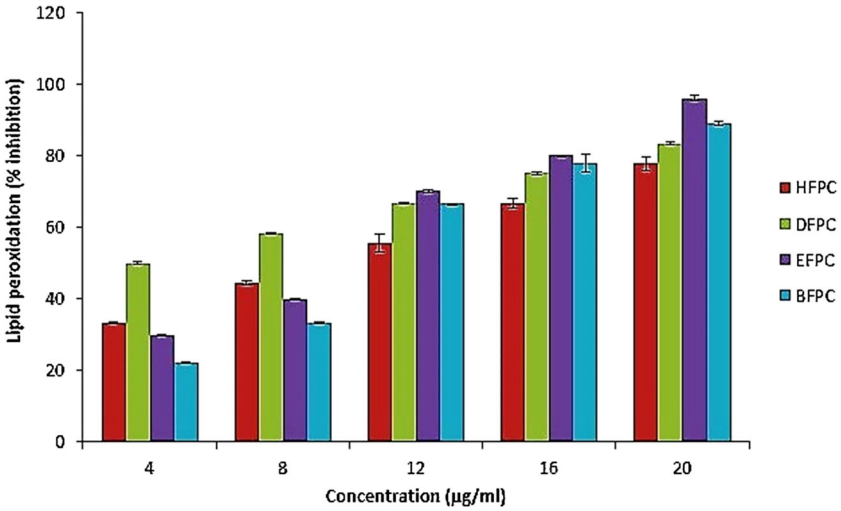

Fig. 3 Effect of different solvent fractions from crude aqueous-methanolic extract of *Parinari curatellifolia* seed on sodium nitroprusside–induced lipid peroxidation in the artery of albino rats in vitro. Results are expressed as mean ± SD ($n = 3$). CMPC, crude aqueous-methanolic extract of *Parinari curatellifolia* seed; HFPC, n-hexane fraction from CMPC; DFPC, dichloromethane fraction from CMPC; EFPC, ethyl acetate fraction from CMPC; BFPC, n-butanol fractions from CMPC

Jenway, Barlo World Scientific, Dunmow, United Kingdom) were used to centrifuge and measure the absorbance respectively.

Preparation of crude aqueous-methanolic extracts and fractions

Dried seeds of *P. curatellifolia* were obtained from Oja-Oba market in Akure, Nigeria, in June 2017. Botanical identification and authentication were carried out and the voucher specimen (PC005) was deposited in the Department of Biochemistry, Federal University of Technology Akure, Nigeria. One thousand grams (1000 g) of the seeds was grated using a mesh and then extracted by maceration in 2 l of 80% (v/v) methanol for 48 h. The mixture was filtered and the filtrate obtained was concentrated using a rotary evaporator and then freeze-dried to obtain the crude extract *of P. curatellifolia* (CMPC). Part of the CMPC was mixed with water and fractioned sequentially using hexane (HFPC), dichloromethane (DFPC), ethyl acetate (EFPC), and n-butanol (BFPC). The fractions were evaporated to dryness using a rotary evaporator. The crude extract and fractions were stored in a desiccator at 4 °C.

Phytochemical screening

The crude extract as well as the fractions (n-hexane, dichloromethane, ethyl acetate, and n-butanol) of CMPC was qualitatively examined for the presence of phytochemicals using the standard method (Sofowora 1993).

Animals

Adult male Wistar rats weighing 160 ± 10 g were used for the study and were obtained from the animal breeding house by the Department of Biochemistry, Federal University of Technology, Akure, Nigeria. The animals were housed under controlled light cycle (12 h light/12 h dark) and were fed with

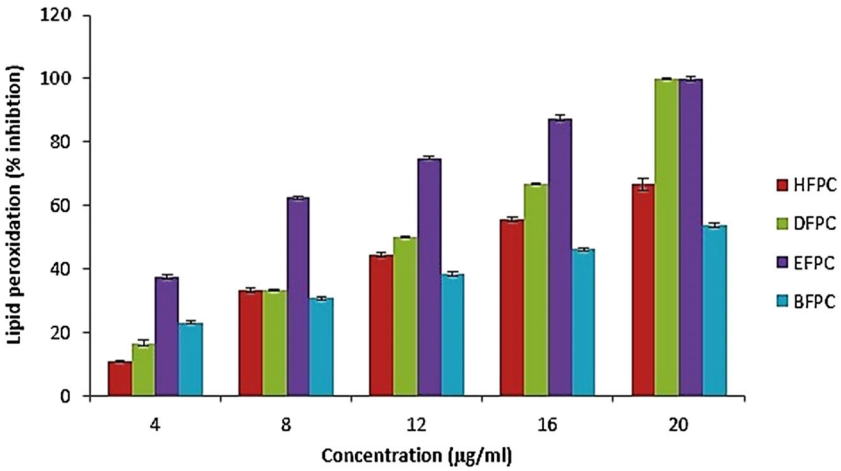

Fig. 4 Effect of different solvent fractions from crude aqueous-methanolic extract of *Parinari curatellifolia* seed on sodium nitroprusside–induced lipid peroxidation in the heart of albino rats in vitro. Results are expressed as mean ± SD ($n = 3$). CMPC, crude aqueous-methanolic extract of *Parinari curatellifolia* seed; HFPC, n-hexane fraction from CMPC; DFPC, dichloromethane fraction from CMPC; EFPC, ethyl acetate fraction from CMPC; BFPC, n-butanol fractions from CMPC

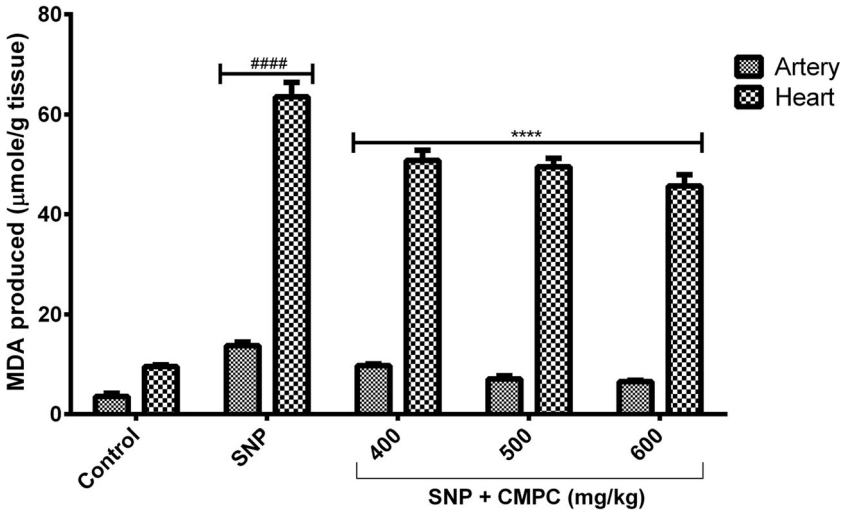

Fig. 5 Effect of crude aqueous-methanolic extract of *Parinari curatellifolia* seed on sodium nitroprusside–induced lipid peroxidation in the artery and heart of albino rats in vivo. Results are expressed as mean ± SD ($n = 6$). $^{####}p < 0.0001$ vs control, $^{****}p < 0.0001$ vs induced. CMPC, crude aqueous-methanolic extract of *Parinari curatellifolia* seed; SNP, sodium nitroprusside; MDA, malonyldialdehyde

commercial rat chow obtained from Vital Feeds Nigeria Limited ad libitum, and liberally supplied with water. All animal experiments were conducted according to the guidelines of the National Institute of Health (NIH publication 85-23, 1985) for laboratory animal care and use.

In vitro assay

Preparation of homogenate from rat organs

Animals were sacrificed under ether anesthesia and the heart and coronary artery were removed. The organs were quickly rinsed in ice-cold saline, blotted with a filter paper, and weighed. The organs were then chopped into bits using dissecting set stainless scissors and homogenized in ten volumes of phosphate-buffered saline (50 mM, pH 7.4) using a Teflon homogenizer. The homogenate was centrifuged at 3000×*g* for 10 min. The pellet was discarded and the low speed supernatant obtained was used for lipid peroxidation assay.

Evaluation of protection by *P. curatellifolia* against sodium nitroprusside–induced lipid peroxidation in the heart and artery of rats

A modified method of Ohkawa et al. (1979) was used to evaluate lipid peroxidation inhibitory activity. The homogenate supernatant of rat organs (0.1 ml) was added to 0.03 ml of various concentrations of crude extract or fractions inside the screw-covered test tube. The volume was made up to 1 ml with distilled water. Thereafter, 0.03 ml of 5 mM SNP was

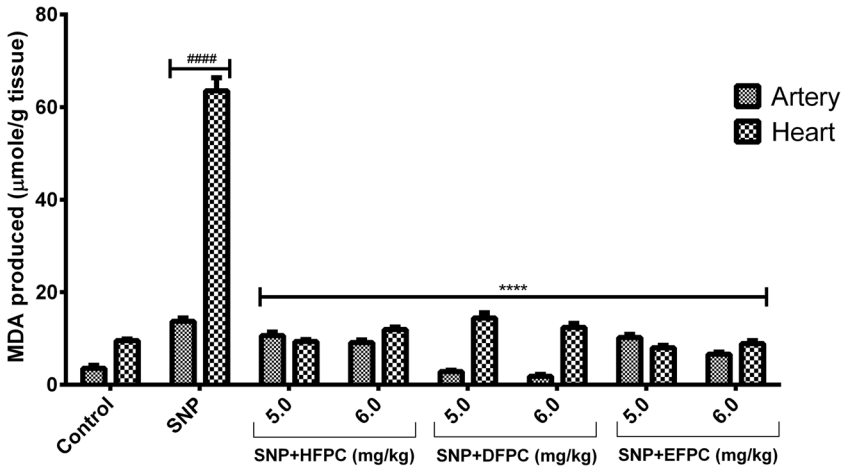

Fig. 6 Effect of different solvent fractions from crude aqueous-methanolic extract of *Parinari curatellifolia* seed on sodium nitroprusside–induced lipid peroxidation in the artery and heart of albino rats in vivo. Results are expressed as mean ± SD ($n = 6$). $^{####}p < 0.0001$ vs control, $^{****}p < 0.0001$ vs SNP. CMPC, crude aqueous-methanolic extract of *Parinari curatellifolia* seed; HFPC, n-hexane fraction from CMPC; DFPC, dichloromethane fraction from CMPC; EFPC, ethyl acetate fraction from CMPC; BFPC, n-butanol fractions from CMPC; SNP, sodium nitroprusside; MDA, malonyldialdehyde

Table 2 Effect of crude aqueous-methanolic extract of *Parinari curatellifolia* seed post-treatment on biochemical indices in serum of rats intoxicated with sodium nitroprusside

Groups	AST (U/L)	ALT (U/L)	BIL (μmol/L)	CREA (μmmol/L)	UREA (mmol/L)	UA (μmol/L)
Control	5.07 ± 1.27	5.84 ± 0.28	12.49 ± 0.13	68.50 ± 5.20	15.973 ± 0.28	290.58 ± 6.5
SNP	11.71 ± 1.39$^{\#\#\#\#}$	9.31 ± 0.85$^{\#\#\#\#}$	36.91 ± 1.96$^{\#\#\#\#}$	324.75 ± 0.35$^{\#\#\#\#}$	60.84 ± 0.81$^{\#\#\#\#}$	1065.08 ± 15.81$^{\#\#\#\#}$
SNP + CMPC (400 mg/kg)	7.97 ± 0.48****	7.29 ± 0.22****	32.10 ± 1.18****	231.25 ± 6.72****	20.10 ± 0.98****	882.52 ± 21.79****
SNP + CMPC (500 mg/kg)	5.65 ± 0.46****	7.85 ± 0.17**	23.68 ± 1.31****	147.75 ± 0.35****	29.07 ± 0.04****	562.15 ± 0.79****
SNP + CMPC (600 mg/kg)	4.76 ± 0.64****	8.35 ± 0.98	13.04 ± 0.28****	88.00 ± 0.71****	33.42 ± 1.86****	411.94 ± 2.03****

Results are expressed as mean ± SD ($n = 6$). $^{\#\#\#\#}p < 0.0001$ vs control, $^{**}p < 0.01$, $^{****}p < 0.0001$ vs SNP. *CMPC* crude aqueous-methanolic extract of *Parinari curatellifolia* seed, *SNP* sodium nitroprusside, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *BIL* bilirubin, *CREA* creatinine, *UA* uric acid

added and the mixture was incubated for 60 min at 37 °C. Then, 0.5 ml acetic acid (1.34 M, pH 3.4) was added, followed by 0.5 ml of 0.8% w/v TBA and 0.3 ml of 8.1% SDS. The resulting mixture was vortexed and incubated at 100 °C for 60 min inside the screw-covered test tube. After cooling, 5 ml of n-butanol was added and the mixture was centrifuged at 3000×*g* for 10 min. The absorbance of the organic upper layer was measured at 532 nm and converted to percentage inhibition using the formula $(1 - E/C) \times 100$, where C is the absorbance of fully oxidized control and E is the absorbance in the presence of the extract or its fractions.

In vivo assay

Experimental design

Male Wistar rats weighing 160 ± 10 g were used. Animals were divided into 2 sections (A and B).

Section A consists of five (5) groups of six (6) animals each; group A1 served as the negative control and received distilled water alone; group A2 served as the positive control and the rats in this group were administered SNP (5 mg/kg bwt) only while groups A3–A5 were also administered SNP (5 mg/kg bwt) and were later treated with CMPC (400, 500, and 600 mg/kg bwt) after 12 h, respectively.

Section B consists of four (4) groups of six (6) animals each; groups B1 and B2 served as the negative and positive controls, respectively, while groups B3 and B4 were administered SNP (5 mg/kg bwt) and were later treated with various solvent fractions of CMPC (5 and 6 mg/kg bwt) after 12 h, respectively. All administrations and treatments were carried out orally for 7 days and animals were sacrificed 24 h after the last administration.

N.B.: Groups 3 and 4 under set B were further divided into three sub-groups according to various fractions (HFPC, DFPC, and EFPC) obtained from CMPC used in this study.

Biochemical analyses

The hearts and arteries of the sacrificed rats were excised, washed in ice-cold 1.15% (v/v) potassium chloride solution, blotted with filter paper, and weighed with average weight of

Table 3 Effect of different solvent fractions from crude aqueous-methanolic extract of *Parinari curatellifolia* seed post-treatment on biochemical indices in serum of rats intoxicated with sodium nitroprusside

Groups	AST (U/L)	ALT (U/L)	BIL (μmol/L)	CREA (μmmol/L)	UREA (mmol/L)	UA (μmol/L)
Control	5.07 ± 1.27	5.84 ± 0.28	12.49 ± 0.13	68.50 ± 5.20	15.973 ± 0.28	290.58 ± 6.5
SNP	11.71 ± 1.39$^{\#\#\#\#}$	9.31 ± 0.85$^{\#\#\#\#}$	36.91 ± 1.96$^{\#\#\#\#}$	324.75 ± 0.35$^{\#\#\#\#}$	60.84 ± 0.81$^{\#\#\#\#}$	1065.08 ± 15.81$^{\#\#\#\#}$
SNP + HFPC (5 mg/kg)	5.84 ± 0.98****	4.08 ± 0.37****	23.82 ± 4.62****	132.75 ± 17.03****	27.07 ± 0.85****	569.45 ± 16.28****
SNP + HFPC (6 mg/kg)	9.33 ± 0.34****	4.40 ± 0.12****	19.38 ± 3.06****	61.25 ± 4.50****	31.36 ± 0.66****	359.76 ± 16.85****
SNP + DFPC (5 mg/kg)	6.83 ± 0.01****	6.00 ± 0.00****	23.26 ± 0.95****	177.00 ± 0.42****	26.48 ± 2.10****	278.91 ± 28.35****
SNP + DFPC (6 mg/kg)	5.51 ± 0.00****	6.54 ± 0.00****	29.6 ± 0.66****	169.23 ± 0.16****	52.43 ± 1.95****	170.55 ± 24.91****
SNP + EFPC (5 mg/kg)	4.84 ± 0.00****	6.54 ± 0.01****	17.53 ± 0.32****	51.63 ± 8.24****	6.96 ± 0.29****	476.23 ± 5.80****
SNP + EFPC (6 mg/kg)	5.51 ± 0.00****	6.38 ± 0.01****	24.42 ± 0.40****	59.00 ± 4.09****	15.29 ± 0.28****	364.38 ± 8.40****

Results are expressed as mean ± SD ($n = 6$). $^{\#\#\#\#}p < 0.0001$ vs control, $^{****}p < 0.0001$ vs SNP. *CMPC* crude aqueous-methanolic extract of *Parinari curatellifolia* seed, *HFPC* n-hexane fraction from CMPC, *DFPC* dichloromethane fraction from CMPC, *EFPC* ethyl acetate fraction from CMPC, *BFPC* n-butanol fractions from CMPC, *SNP* sodium nitroprusside, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *BIL* bilirubin, *CREA* creatinine, *UA* uric acid

0.48 ± 0.05 and 0.1 ± 0.01 g, respectively. They were then homogenized in phosphate-buffered saline (50 mM, pH 7.4) (1:10 w/v) using a Teflon homogenizer. The resulting homogenate was centrifuged at 3000×*g* at 4 °C for 30 min to obtain the supernatant, which was used for biochemical analyses. The extent of lipid peroxidation was evaluated by the concentration of malonylaldehyde (MDA) produced (Ohkawa et al. 1979). Blood was collected via cardiac puncture into serum tubes and centrifuged at 4000*g* for 10 min. The clear supernatant was collected and used for estimation of serum biochemical indices; aspartate aminotransferase (AST) and alkaline phosphatase (ALP) activities as well as bilirubin, creatinine, urea, and uric acid levels were estimated using Randox assay kits according to the manufacturer's instructions.

Statistical analysis

Results were expressed as mean ± S.D. ($n = 6$) and analyzed using appropriate analysis of variance (ANOVA) followed by Tukey multiple comparison test for multiple comparisons. In all the tests, $p < 0.05$ was taken as a criterion for statistical significance. The statistical software used to analyze the data was GraphPad Prism 6.01 (GraphPad Software Inc., CA, USA).

Results and discussion

From the phytochemical analysis (Table 1), alkaloids, saponins, tannins, flavonoid, terpenoids, phlobatannin, and cardiac glycosides were detected in CMPC. Terpenoids and steroidal ring of cardiac glycoside were detected in HFPC. Alkaloids and cardenolides of cardiac glycoside were the only phytochemical detected in DFPC, while flavonoids were only found in EFPC. Four phytochemicals (alkaloid, saponin, tannin, and deoxy sugar and cardenolides type of cardiac glycoside) were detected in BFPC.

Reports have shown that these phytochemicals possessed medicinal values; hence, they are responsible for the bioactivity of medicinal plants used in the management of many human ailments (Olaleye et al. 2014; Crown et al. 2016, 2017a, b; Manuwa et al. 2017). For example, saponins, which consist of a triterpene or steroid aglycone with one or more sugar moiety (Khan et al. 2012), have been reported to confer antioxidant, hypolipidemic, and hypoglycemic abilities as well as immune stimulatory potentials (Song et al. 2012; Elekofehinti et al. 2014). Cardiac glycosides involve in the regulation of heart contraction rate by acting on the cellular sodium-potassium ATPase pump (Patel 2016). Alkaloids on the other hand are heterocyclic nitrogen-containing basic compounds that are widely exploited as pharmaceuticals (Doughari 2012; Latif et al. 2017). A handful number of reports have shown that polyphenols (phenolic acid and flavonoids) possessed a wide range of pharmacological activities (Mahomoodally et al. 2012; Olaleye et al. 2014; Akinmoladun et al. 2015). These phytochemicals could be responsible for the various pharmacological importance of *P. curatellifolia*.

The in vitro inhibitory effect of the CMPC, BFPC, DFPC, EFPC, and HFPC on SNP-induced lipid peroxidation in a rat's artery and heart is presented in Figs. 1, 2, 3, and 4, respectively. The result shows that there is a significant ($p < 0.05$) increase in MDA production in SNP-induced artery and heart homogenate compared with the control group. However, treatment with CMPC and the fractions reduced MDA production dose-dependently closer to the control group. However, CMPE exhibited the highest effect at 6 μg/ml on both tissues (Figs. 1 and 2). Figures 3 and 4 represent the effect of the fractions against MDA production induced by SNP in artery and heart homogenate. DFPC exhibited the highest percent inhibition on the artery at 4 and 8 μg/ml (50% and 60%, respectively) when compared with the other fractions, while EFPC at 12, 16, and 20 μg/ml exhibited the highest percent inhibition at 20 μg/ml (88.89%). On the heart, EFPC also had the highest inhibitory effect on MDA production when compared with other fractions at all dosage used. Figures 5 and 6 presented the in vivo effect of the samples on the artery and heart of rats treated with the SNP. The result revealed that there was a significant increase in MDA production in the rat's artery and heart homogenate compared with the normal control. Interestingly, all the SNP-induced rats treated with CMPC and the fractions had reduced MDA level in the heart and artery homogenate. HFPC offered the highest MDA reduction in artery homogenate compared with other fractions, while EFPC elicit the highest effect against MDA production in rat's heart.

The SNP is an antihypertensive drug that acts by relaxing vascular smooth muscle, thus dilates peripheral arteries and veins. However, it has also been reported to cause side effect by acting as pro-oxidant that induced oxidative stress, possibly due to cyanide content and increased/excess released of NO that could interact with peroxynitrite, and initiate lipid peroxidation (Posser et al. 2006; Hottinger et al. 2014), which is evident in this experiment of increasing MDA content in artery and heart homogenate. Interestingly, all the samples mitigate this effect, thus validate the antioxidant activity of the samples and its use in the management of human ailments. The effects could be as a result of its phytoconstituents such as flavonoids and alkaloids, with potentials to protect against lipid peroxidation (Elekofehinti et al. 2015; Saeed et al. 2016; Sabir et al. 2017).

Tables 2 and 3 showed the effect of tested samples on serum biochemical indices of SNP-intoxicated rats. The result revealed that the SNP administration caused a significant increase in the serum AST and ALT activities, including bilirubin, creatinine, urea, and uric acid levels when compared with

the control group. The elevation of these biochemicals in the serum of SNP-intoxicated rats indicates multiple organ (including the heart, liver, and kidney) damage (El-Demerdash and Nasr 2014; Vinod et al. 2018). However, these effects were mitigated by CMPC and the fractions. Comparatively among the fractions, EFPC extract had a higher effect than HFPC and DFPC extracts. Several studies have revealed the protective potentials of plant chemical most especially flavonoid-rich plants (Mahomoodally et al. 2012; Kumar and Pandey 2013; Olaleye et al. 2014; Akinmoladun et al. 2015) and this could be responsible for the protective effect of EFPC against SNP-induced toxicity, compared with other solvent fractions from CMPC.

Conclusion

This study revealed that *P. curatellifolia* is rich in phytochemicals, which could be explored against the side effect of SNP toxicity in the management of hypertension and other related effect, thus could serve as a good therapeutic agent to combat cardiovascular-related complications. However, further study including detailed mechanism of actions(s) on ameliorative effect of *P. curatellifolia* seed extracts should be carry out.

Compliance with ethical standards

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

Ethical approval All institutional and national guidelines for the care and use of laboratory animals were followed.

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