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Ameliorative and antidyslipidemic potentials of aqueous leaf extract of *Gongronema latifolium* in CCl_4 carbon tetrachloride-induced oxidative stress rats

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ABSTRACT

Objective: To investigate the effect of leaf aqueous extract from *Gongronema latifolium* (*G. latifolium*) on CCl_4 induced-oxidative stress in Wistar rat. This effect was assessed by measuring liver marker enzymes activity, analyzing the antioxidant parameters, lipid profile estimation and lipid peroxidation by-product following CCl_4 induced-oxidative stress.

Methods: Milled *G. latifolium* leaves were subjected to aqueous extraction and the filtrate was evaporated between 40–60 ˚C under reduced pressure and a calculated volume of the leaf extract was administered at a dose of 500 mg/kg body weight. Thirty-five rats were grouped into seven groups of 5 animals each namely; control and experimental groups. The experimental groups were treated with 2.0 mL/kg body weight CCl_4, 25 mg/kg body weight/day silymarin (a standard hepatoprotective antioxidant), 500 mg/kg body weight aqueous extract of *G. latifolium* leaves were administered to the CCl_4 treated rats for 21 days.

Results: Administration of the extract and silymarin increase significantly ($P < 0.05$) in liver marker enzyme (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and gamma-glutamyl transpeptidase) activities in serum, liver and kidney in the treated groups when compared with untreated groups. The antioxidant parameters (catalase, peroxidase and glutathione *S*-transferase) were significantly elevated ($P < 0.05$) in animals treated with the extract and silymarin in comparison with untreated groups. CCl_4 induced oxidative stress mediated variations in total cholesterol, triacylglycerides, high-density lipoprotein cholesterol, low density lipoprotein cholesterol and very low-density lipoprotein cholesterol were restored significantly ($P < 0.05$) by the extract.

Conclusions: The result obtained from this study indicated the antioxidant and antidyslipidemic potentials of the aqueous extract of *G. latifolium* leaves.

1. Introduction

Oxidative stress occurs as a result of an imbalance between formation and neutralization of reactive oxygen species and/or reactive nitrogen species[1]. It plays a major part in the manifestation of chronic and degenerative ailments such as cancer, autoimmune disorders, rheumatoid arthritis, cataract, aging, cardiovascular and neurodegenerative diseases[2,3]. CCl_4 is a small, lipophilic molecule that spreads easily in the lipid compartments of the body and is metabolized in the liver. Its mode of toxicity requires a cytochrome P450-mediated biotransformation step. Cytochome P450 2E1 which produces free radicals, such as trichloromethyl (CCl_3)[4], and induces the peroxidation of lipids. The CCl_3 undergoes biotransformation into a more reactive CCl_3O_2 which also not peroxidizes lipid but disturb Ca^{2+} homeostasis and eventually kill cells[5]. Administration of CCl_4 in rats elevates hepatic protein oxidation which results in the accumulation of oxidized proteins in the liver[6]. CCl_4 ingestion and metabolism in the liver generates free radicals which in turn, trigger a cascade of events resulting in hepatic fibrosis.

Ethanol has been known to induce oxidative stress but the major pathway appears to be cytochrome P450 2E1 induction which metabolizes and activates many toxicological substrates including ethanol, CCl_4, *etc*. to more reactive toxic end products. The levels of cytochome P450 2E1 are usually augmented in physiological condition after an exposure to either acute or chronic alcohol treatment.

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All experimental procedures involving animals were conducted in accordance to Ethical Committee on the Use and Care of Animals of Al-Hikmah University Ilorin and approved by Ethical Committee.

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Certain tropical plants have been proposed to have medicinal value and the variety of local herbs and vegetables by human consumption is believed to contribute significantly to the improvement of human health, in terms of prevention, and or cure of diseases since plants have long served as a useful and natural source of therapeutic agents[7]. One of such plant is *Gongronema latifolium* (*G. latifolium*).

G. latifolium is an herbaceous non-woody plant belonging to the family of Asclepiadaceae. It has milky or clear latex, widespread in tropical and subtropical regions especially in Africa and South America, with a moderate representation in Northern and Southeastern Asia[8]. In Southeastern and Western Nigeria, *G. latifolium* (whose leaves are bitter) is called "utazi" and "arokeke", respectively, and is used as spice and vegetables in traditional folk medicine[9]. Earlier reports on extract from this plant have focused mainly on their medicinal properties[10,11], with little attempt in investigating their ameliorative and antidyslipidemic potentials. Sabinus and Bennett reported its use as bittering agents in brewing to produce the characteristic flavour, foam stability, and preservative properties in beer[9]. Adenuga *et al*.[12] have used Nigerian bitter vegetables of *G. latifolium*, *Vernonia amygdalina*, and *Garcinia kola* as substitutes for commercial hops in lager beer production.

2. Materials and methods

2.1. Plant material and authentication

G. latifolium leaf was procured from Mushin market, Lagos, Lagos State, Nigeria. The plant was authenticated at Bioresources Development and Conservation Programme, Nsukka, Southeastern Nigeria and a voucher number (INTERCEDD/170) was deposited at the center.

2.2. Chemicals and reagents

Assay kits of high density lipoprotein (HDL), low density lipoprotein (LDL), very LDL (VLDL), total cholesterol, triglycerides, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphates (ALP) and gamma glutamyltransferase (GGT) were products of Randox Laboratory Ltd. (Co Antrim, UK) Silymarin was a peoduct of Aromokeye Pharmaceuticals Limited, Kwara State, Nigeria. All other chemicals and reagents were of analytical grade and were prepared in glass wares.

2.3. Preparation of aqeuous extract of G. latifolium

Fresh *G. latifolium* leaves were oven dried at 40 ˚C and pulverized in a blender (Binatone blender, mode BLG-699) and the resulting powder (500 g) was soaked in 2 L distilled water at room temperature for 24 h. The mixture was filtered using a muslin cloth and the resulting filtrate was concentrated using rotary evaporator under reduced pressure to give a semi solid residue which is then dried using the oven at 60 ˚C to get a greenish powder.

2.4. Animals

Thirty-five male albino Wistar rats with body weight ranging from 150 to 180 g were used for the study. Animals were obtained from the animal holding unit of the Department of Biochemistry, University of Ilorin, Kwara State, Nigeria. The animals were kept in clean and well ventilated plastic cages at normal temperature and fed pellet diet and water *ad libitum*. This study was carried out following the approval from the Ethical Committee on the Use and Care of Animals of Al-Hikmah University Ilorin, Nigeria and an ethical clearance number HUI/ECULA/014/003.

2.5. Experimental design

A completely randomized experimental design was adopted for the study. Thirty-five male Albino rats body weight ranges from 150–180 g were randomized into seven groups of five rats each after acclimatization for a week. They were fed *ad libitum* with normal diet and alcohol (10%) in drinking water.

2.6. Treatment groups

The oxidant (CCl_4) was used to induce stress *in vivo*, which undergoes metabolic activation to the oxidative moiety by cytochome P450 2E1. The animals treated with the oxidant to induce cytochome P450 2E1 activity were pre-treatment with alcohol (10%) in drinking water for 20 days. CCl_4 was administered as a single subcutaneous injection (2.0 mL/kg body weight) diluted 1:1 in paraffin oil on the 21st day. Aqueous leaf extract of *G. latifolium* was administered at a dose of 500 mg/kg body weight. The experimental design was as follows:

Group I was the control group. Group II was treated with alcohol control; Group III was administrated with alcohol + CCl_4; Group IV received alcohol + 500 mg/kg body weight of aqueous leaf extract of *G. latifolium*; Group V was treated with alcohol + 500 mg/kg body weight of aqueous leaf extract of *G. latifolium* + CCl_4; Group VI received alcohol + 25 mg/kg body weight of silymarin; Group VII was given alcohol + 25 mg/kg body weight of silymarin + CCl_4.

A standard hepatoprotective antioxidant (silymarin) was given at a dose of 25 mg/kg body weight per day. The extract and silymarin were administered *p.o.* (oral gavage) for 21 days. After the treatment for 21 days, the animals were sacrificed on the 22nd day by cervical dislocation and blood was collected through jugular puncture. Serum was separated by centrifugation at 2 500 r/min at room temperature. Serum and tissue samples were analyzed for liver marker enzymes, antioxidant parameters, lipid profile and lipid peroxidation by-product.

2.7. Liver marker enzymes assay

The liver damage marker enzymes, namely ALT, AST[13,14], ALP and GGT[15] were estimated in the tissue and serum samples. The enzymes were assayed using Randox kits obtained from Randox laboratories, UK.

2.8. Estimation of antioxidant parameters

The level of catalase activity was assayed following the method of Luck[16]. The method proposed by Reddy *et al*.[17] was adopted for assaying the activity of peroxidase. Glutathione *S*-transferase was assessed by the method of Habig *et al*.[18].

2.9. Estimation of lipid profile

The levels of cholesterol was assayed for using enzymatic colorimetric diagnostic kits obtained from Randox laboratories, UK in which the glycerol phosphate oxidase method[19] was employed. Triacylglycerol (TAG) was determined using the procedure of Jacob and van Damark[20]. The phosphotungstate precipitation method of Richmond[21] as applied in Randox kit was used for the determination of HDL-cholesterol. LDL cholesterol was calculated as: LDL (mmol/L) = Total cholesterol triglycerides/2.2 – HDL, while VLDL-cholesterol was estimated as: VLDL (mmol/L) = Triglyceride/2.2.

2.10. Lipid peroxidation assay

The concentration of malondialdehyde was quantified according to the procedure by Reilly and Aust[22].

2.11. Statistical analysis

Data were analyzed by the use of the analysis of variance procedure implemented within, SPSS version 16. Significantly different means was separated by the use of Tukey multiple comparison test, also within SPSS 16.

3. Result

3.1. Effect of aqueous leaf extract of G. latifolium on liver marker enzymes

Tables 1, 2 and 3 show the effect of aqueous leaf extract of *G. latifolium* on AST, ALT, ALP and GGT activities in (serum, liver and kidney) respectively of CCl_4 induced oxidative stress rats. The activities of hepatic and renal AST, ALT, GGT and ALP in extract and silymarin treated rats were shown in Tables 1 and 2 respectively. Following the administration of the extract and silymarin, a significant increase ($P < 0.05$) in the activities of AST, ALT, GGT and ALP was observed when compared with untreated group. However, the result in Table 3 shows significant increase ($P < 0.05$) in serum activities of AST, ALT, GGT and ALP of untreated groups when compared with the control. Also, treatment with the extract and silymarin revealed a significant decrease ($P < 0.05$) when compared with untreated groups.

3.2. Effect of aqueous leaf extract of G. latifolium on antioxidant parameters

Figures 1–3 show the effect of aqueous leaf extract of *G. latifolium* on antioxidant parameters of CCl_4 induced oxidative stress rats. The activity of catalase, peroxidase and glutathione *S*-transferase in serum, liver and kidney tissues were significantly reduced ($P < 0.05$) in untreated animals when compared with the control. Upon treatment with the extract and silymarin, a significant increase ($P < 0.05$) was observed when compared with untreated groups.

3.3. Effect of aqueous leaf extract of G. latifolium on lipid profile

Tables 4, 5 and 6 show the effect of aqueous leaf extract of *G. latifolium* on HDL, LDL, VLDL, TAG and cholesterol levels in liver, kidney and serum respectively of CCl_4 induced oxidative stress rats. The result revealed a significant increase ($P < 0.05$) in TAG, LDL and VLDL levels in untreated groups when compared with the control but upon administration of the extract and silymarin, there was a significant increase ($P < 0.05$) when compared with untreated groups. However, a significant decrease ($P < 0.05$) was revealed in HDL and cholesterol levels in untreated groups when compared with the control but upon administration of the extract and silymarin, there was a significant decrease ($P < 0.05$) when compared with untreated groups.

3.4. Effect of aqueous leaf extract of G. latifolium on malondialdehyde concentration

Figure 4 shows the effect of aqueous leaf extract of *G. latifolium* on malondialdehyde concentration on CCl_4 induced oxidative stress

Table 1
Effect of aqueous leaf extract of *G. latifolium* on serum AST, ALT, ALP and GGT activities in serum of CCl_4 induced oxidative stress rats.

Serum	AST	ALT	ALP	GGT
Control	100.150 ± 0.024^{a}	201.340 ± 0.065^{e}	257.830 ± 0.000^{a}	173.400 ± 0.021^{a}
Alcohol control	270.160 ± 0.024^{c}	92.030 ± 0.090^{b}	709.340 ± 0.000^{d}	335.340 ± 0.016^{d}
Alcohol + CCl_4	291.320 ± 0.029^{c}	73.650 ± 0.070^{a}	722.430 ± 0.000^{d}	323.340 ± 0.016^{d}
Alcohol + *G. latifolium* (500 mg)	108.450 ± 0.016^{a}	194.560 ± 0.057^{d}	386.860 ± 0.000^{c}	210.440 ± 0.024^{b}
Alcohol + CCl_4 + *G. latifolium* (500 mg)	110.740 ± 0.016^{a}	188.930 ± 0.101^{d}	393.470 ± 0.000^{c}	221.480 ± 0.026^{b}
Alcohol + silymarin	128.070 ± 0.029^{b}	176.830 ± 0.115^{c}	333.100 ± 0.000^{b}	235.340 ± 0.021^{c}
Alcohol + CCl_4 + silymarin	108.230 ± 0.024^{a}	172.990 ± 0.107^{c}	401.880 ± 0.000^{c}	230.560 ± 0.024^{c}

Table 2
Effect of aqueous leaf extract of *G. latifolium* on liver AST, ALP, GGT and ALT activities in serum of CCl_4 induced oxidative stress rats.

Liver	AST	ALT	ALP	GGT
Control	291.160 ± 0.009^{d}	187.450 ± 0.070^{e}	725.680 ± 0.000^{e}	275.220 ± 0.024^{d}
Alcohol control	129.570 ± 0.002^{a}	92.770 ± 0.096^{b}	218.270 ± 0.000^{a}	163.620 ± 0.024^{a}
Alcohol + CCl_4	120.950 ± 0.068^{a}	69.890 ± 0.111^{a}	222.430 ± 0.000^{a}	155.620 ± 0.024^{a}
Alcohol + *G. latifolium* (500 mg)	264.160 ± 0.008^{c}	179.450 ± 0.053^{e}	713.190 ± 0.000^{e}	262.820 ± 0.013^{c}
Alcohol + CCl_4 + *G. latifolium* (500 mg)	223.190 ± 0.064^{b}	165.980 ± 0.112^{d}	679.420 ± 0.000^{d}	249.930 ± 0.024^{c}
Alcohol + silymarin	250.080 ± 0.010^{c}	162.870 ± 0.094^{d}	608.950 ± 0.000^{c}	250.110 ± 0.024^{c}
Alcohol + CCl_4 + silymarin	218.830 ± 0.012^{b}	145.900 ± 0.070^{c}	556.370 ± 0.000^{b}	226.280 ± 0.024^{b}

Table 3

Effect of aqueous leaf extract of *G. latifolium* on kidney AST, ALP, GGT and ALT activities in serum of CCl_4 induced oxidative stress rats.

Kidney	AST	ALT	ALP	GGT
Control	209.180 ± 0.006[d]	103.980 ± 0.016[e]	756.260 ± 0.008[d]	212.510 ± 0.005[c]
Alcohol control	116.060 ± 0.006[a]	46.870 ± 0.017[b]	289.340 ± 0.008[a]	160.840 ± 0.046[a]
Alcohol + CCl_4	103.130 ± 0.006[a]	32.160 ± 0.024[a]	281.370 ± 0.008[a]	148.840 ± 0.015[a]
Alcohol + *G. latifolium* (500 mg)	195.120 ± 0.006[c]	98.920 ± 0.108[d]	724.350 ± 0.005[d]	196.680 ± 0.005[b]
Alcohol + CCl_4 + *G. latifolium*	180.060 ± 0.006[b]	90.010 ± 0.802[d]	675.530 ± 0.008[c]	193.720 ± 0.007[b]
Alcohol + silymarin	190.000 ± 0.006[c]	88.920 ± 0.031[d]	648.600 ± 0.004[c]	187.310 ± 0.083[b]
Alcohol + CCl_4 + silymarin	169.100 ± 0.006[b]	75.340 ± 0.103[c]	555.930 ± 0.006[b]	190.030 ± 0.048[b]

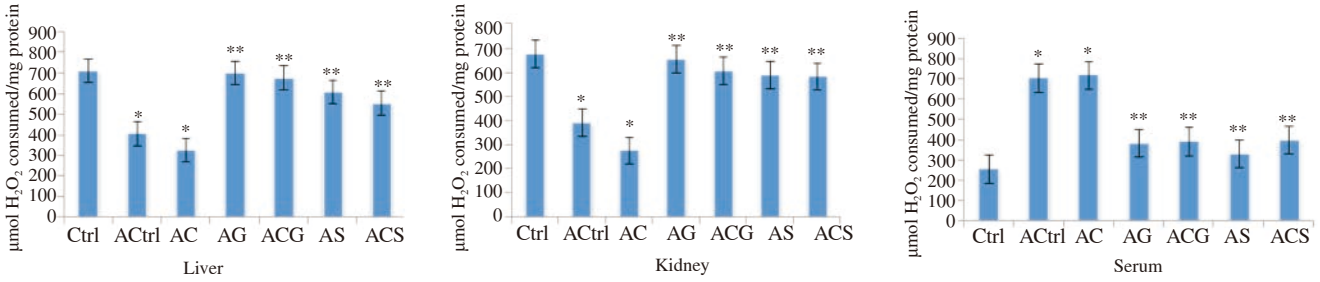

Figure 1. Effect of aqueous leaf extract of *G. latifolium* on specific activity of catalase on serum, liver and kidney tissues of CCl_4 induced-oxidative stress rats. Ctrl: Control; ACtrl: Alcohol control; AC: Alcohol + CCl_4; AG: Alcohol + *G. latifolium* (500 mg); ACG: Alcohol + CCl_4 + *G. latifolium*; AS: Alcohol + silymarin; ACS: Alcohol + CCl_4 + silymarin.

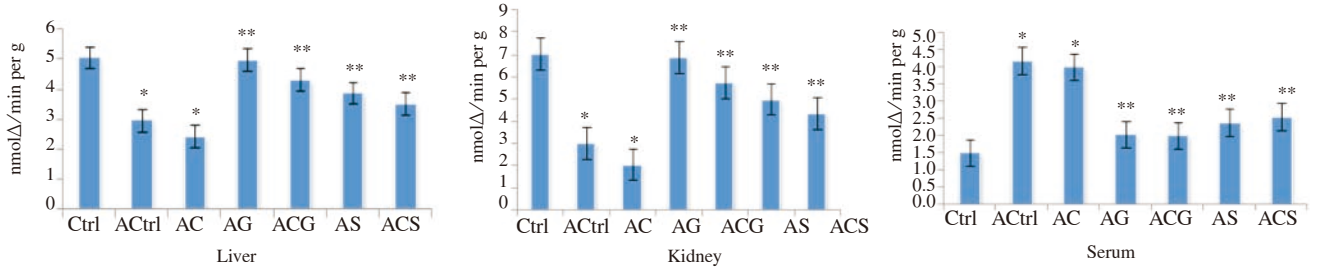

Figure 2. Effect of aqueous leaf extract of *G. latifolium* on specific activity of peroxidase on serum, liver and kidney tissues of CCl_4 induced-oxidative stress rats. Ctrl: Control; ACtrl: Alcohol control; AC: Alcohol + CCl_4; AG: Alcohol + *G. latifolium* (500 mg); ACG: Alcohol + CCl_4 + *G. latifolium*; AS: Alcohol + silymarin; ACS: Alcohol + CCl_4 + silymarin.

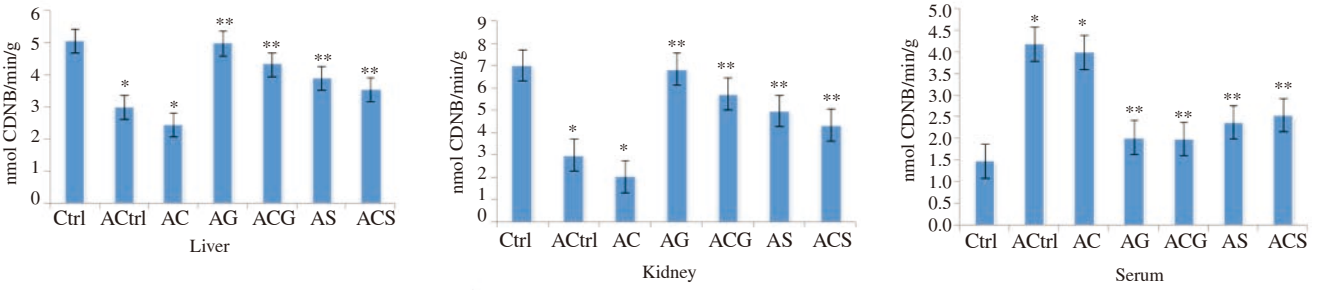

Figure 3. Effect of aqueous leaf extract of *G. latifolium* on specific activity of glutathione *S*-transferase on serum, liver and kidney tissues of CCl_4 induced-oxidative stress rats. Ctrl: Control; ACtrl: Alcohol control; AC: Alcohol + CCl_4; AG: Alcohol + *G. latifolium* (500 mg); ACG: Alcohol + CCl_4 + *G. latifolium*; AS: Alcohol + silymarin; ACS: Alcohol + CCl_4 + silymarin.

Table 4

Effect of aqueous leaf extract of *G. latifolium* on liver HDL, LDL, VLDL, TAG and cholesterol of CCl_4 induced-oxidative stress rats.

Liver	HDL	LDL	VLDL	TAG	Cholesterol
Control	48.750 ± 0.007[b]	159.700 ± 0.030[b]	192.340 ± 0.019[c]	197.020 ± 0.039[c]	5.050 ± 0.017[b]
Alcohol control	27.360 ± 0.006[a]	211.200 ± 0.016[c]	259.330 ± 0.023[d]	213.140 ± 0.040[c]	2.360 ± 0.005[a]
Alcohol + CCl_4	21.750 ± 0.004[a]	226.200 ± 0.021[d]	286.070 ± 0.025[d]	222.120 ± 0.043[c]	2.780 ± 0.005[a]
Alcohol + *G. latifolium* (500 mg)	45.040 ± 0.015[b]	158.900 ± 0.028[b]	152.120 ± 0.012[b]	154.320 ± 0.034[b]	4.970 ± 0.015[b]
Alcohol + CCl_4 + *G. latifolium* (500 mg)	42.360 ± 0.011[b]	137.320 ± 0.026[b]	120.320 ± 0.003[a]	122.120 ± 0.024[a]	4.620 ± 0.012[b]
Alcohol + silymarin	44.650 ± 0.014[b]	128.350 ± 0.024[a]	131.530 ± 0.005[a]	131.440 ± 0.024[a]	4.360 ± 0.009[b]
Alcohol + CCl_4 + silymarin	40.090 ± 0.010[b]	117.070 ± 0.024[a]	111.110 ± 0.007[a]	120.020 ± 0.029[a]	4.060 ± 0.008[b]

Values were expressed as mean ± SEM ($n = 5$). Values with different superscripts down the row are significantly different at $P < 0.05$.

Table 5

Effect of aqueous leaf extract of *G. latifolium* on kidney HDL, LDL, VLDL, TAG and cholesterol of CCl_4 induced-oxidative stress rats

Kidney	HDL	LDL	VLDL	TAG	Cholesterol
Control	46.750 ± 0.018^b	208.540 ± 0.010^b	243.740 ± 0.018^c	279.820 ± 0.024^b	5.950 ± 0.012^b
Alcohol control	27.360 ± 0.009^a	292.420 ± 0.016^c	312.270 ± 0.023^d	303.840 ± 0.029^c	2.360 ± 0.004^a
Alcohol + CCl_4	21.750 ± 0.008^a	299.180 ± 0.018^c	343.880 ± 0.028^d	354.880 ± 0.039^d	2.780 ± 0.003^a
Alcohol + *G. latifolium* (500 mg)	45.040 ± 0.018^b	205.880 ± 0.009^b	206.840 ± 0.013^b	241.820 ± 0.016^a	5.570 ± 0.096^b
Alcohol + CCl_4 + *G. latifolium* (500 mg)	44.360 ± 0.016^b	185.110 ± 0.006^a	198.170 ± 0.007^a	233.330 ± 0.011^a	5.120 ± 0.089^b
Alcohol + silymarin	43.650 ± 0.016^b	182.150 ± 0.003^a	200.090 ± 0.011^b	229.380 ± 0.016^a	5.030 ± 0.086^b
Alcohol + CCl_4 + silymarin	41.090 ± 0.015^b	176.430 ± 0.001^a	189.100 ± 0.005^a	217.080 ± 0.013^a	4.860 ± 0.086^b

Values were expressed as mean ± SEM (n = 5). Values with different superscripts down the row are significantly different at $P < 0.05$.

Table 6

Effect of aqueous leaf extract of *G. latifolium* on serum HDL, LDL, VLDL, TAG and cholesterol of CCl_4 induced-oxidative stress rats.

Serum	HDL	LDL	VLDL	TAG	Cholesterol
Control	190.200 ± 0.018^c	167.260 ± 0.016^a	42.560 ± 0.007^a	77.140 ± 0.024^a	4.900 ± 0.006^a
Alcohol control	85.750 ± 0.004^a	228.840 ± 0.022^c	117.010 ± 0.022^b	133.200 ± 0.016^b	18.440 ± 0.020^c
Alcohol + CCl_4	78.080 ± 0.005^a	279.720 ± 0.029^d	123.760 ± 0.025^b	143.240 ± 0.033^c	15.550 ± 0.014^b
Alcohol + *G. latifolium* (500 mg)	179.180 ± 0.016^c	196.070 ± 0.004^b	100.010 ± 0.022^b	127.300 ± 0.028^b	6.540 ± 0.004^a
Alcohol + CCl_4 + *G. latifolium* (500 mg)	160.050 ± 0.110^b	189.970 ± 0.004^b	102.560 ± 0.020^b	127.300 ± 0.024^b	6.230 ± 0.007^a
Alcohol + silymarin	153.020 ± 0.009^b	190.520 ± 0.008^b	52.890 ± 0.004^a	87.180 ± 0.024^a	5.110 ± 0.007^a
Alcohol + CCl_4 + silymarin	121.300 ± 0.008^b	187.990 ± 0.004^b	109.660 ± 0.018^b	130.700 ± 0.031^b	4.820 ± 0.007^a

Values were expressed as mean ± SEM (n = 5). Values with different superscripts down the row are significantly different at $P < 0.05$.

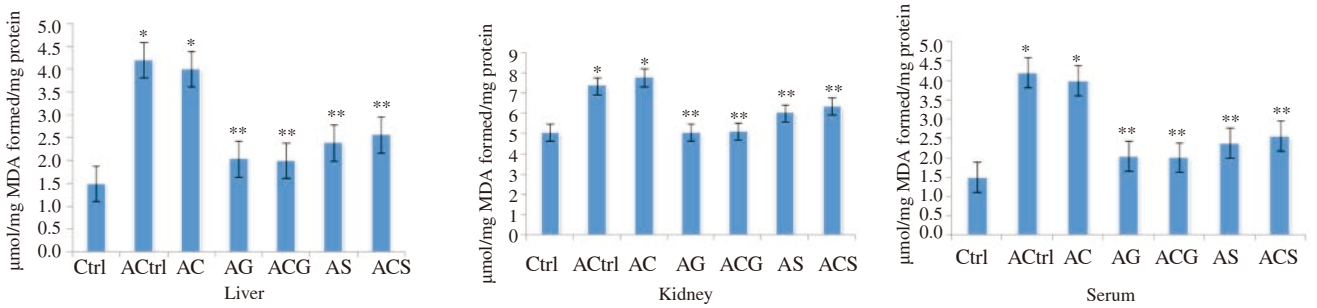

Figure 4. Effect of aqueous leaf extract of *G. latifolium* on malondialdehyde concentration on serum, liver and kidney tissues of CCl_4 induced-oxidative stress rats. Ctrl: Control; ACtrl: Alcohol control; AC: Alcohol + CCl_4; AG: Alcohol + *G. latifolium* (500 mg); ACG: Alcohol + CCl_4 + *G. latifolium*; AS: Alcohol + silymarin; ACS: Alcohol + CCl_4 + silymarin. MDA: malondialdehyde;

rats. The concentration of malondialdehyde in serum, liver and kidney tissues were significantly increased ($P < 0.05$) in untreated animals when compared with the control. Upon treatment with the extract and silymarin, there was a significant decrease ($P < 0.05$) when compared with untreated groups.

4. Discussion

The major role played by the liver is in the maintenance of lipid homeostasis but the presence of radicals generated through oxidative stress may disturb the concentration of lipids in the serum which could be an increased risk factor for atherosclerosis, since elevated LDLc and reduction of HDLc are risk factors of related cardiovascular diseases and atherosclerosis[23].

The decreased activities of AST, GGT, ALT and ALP in the CCl_4 induced rats may indicate necrosis and the integrity of liver cells may also have been compromised. The increased activities observed in AST, GGT, ALT and ALP in rats treated with aqeuous *G. latifolium* leaf extract compared to the untreated group might be attributed to the possibility of the extract to prevent liver damage. This may be that the phytochemicals and antioxidant constituents in *G. latifolium* leaf may have biotransformed the metabolism of CCl_4 to less toxic product. This might have decreased the over production of free radicals generated and augment the activities of radical scavengers[24], minimizing oxidative injury.

Antioxidant marker enzymes (peroxidase, catalase and glutathione *S*-transferase) protect the integrity of the membrane, extracellular fluid components and other marker enzymes from oxidative stress by catalyzing the reduction of lipid peroxide, hydrogen peroxide and organic hydroperoxide[25]. The generation of radical anions by CCl_4 induction was evident from the significant decrease ($P < 0.05$) observed in activities of peroxidase, catalase and glutathione *S*-transferase in the untreated groups. The elevated activity of peroxidase, catalase and glutathione *S*-transferase in the groups treated with the extract may signify a team of defense against reactive oxygen species[26]. The elevated activities of peroxidase, catalase and glutathione *S*-transferase in the group treated with the extract when compared with the untreated group suggest a protective ability of *G. latifolium* leaf extract. This protective effect may be due to the bioactive constituents and other antioxidative components present in *G. latifolium* leaf[27]. Lipid peroxidation, the most important effect of radical activity produces malondialdehyde[28]. The result revealed that CCl_4 significantly increased the concentration of malondialdehyde in the untreated group which lead to glutathione oxidation and consequently depletion of adenosine triphosphate and nicotinamide adenine dinucleotide phosphate which is responsible

for the disruption in synthesis and transport of lipid. Free radicals may be responsible for oxidative damage to cellular compounds such as DNA, carbohydrate, protein and lipid due to suppressed antioxidant defense system[29].

The significant increase in serum very low density lipoprotein, TAG and low density lipoprotein-cholesterol, the concentrations in the untreated groups may be an index of disruption in lipid metabolism. Membrane lipid peroxidation may have distorted liver enzymes activity involved in cholesterol metabolism and lipoprotein formation leading to increase total serum total cholesterol, LDL, VLDL and triglycerides. HDLc concentration decreased in untreated group when compared to the treated groups. This unconventional fluctuation seen in serum lipid may be due to liver damage, causing tissue to compromise its effectiveness in lipid metabolism regulation[25]. Therefore, there is a possibility that CCl_4 exposure predisposed the animals to atherosclerotic conditions. The near normalcy attainment in the HDLc concentration in the treated groups support hypolipidemic potential of *G. latifolium*.

In can be concluded from the results obtained, that CCl_4 induced oxidative stress in rats and disrupt the activity of antioxidant enzymes (peroxidase, catalase and glutathione *S*-transferase), liver marker enzymes (AST, GGT, ALP and ALT), lipid peroxidation by-product (malondialdehyde) and level of lipid profile (VLDL, LDL, total cholesterol, HDL and triglycerides). *G. latifolium* leaf was able to restore the activity of the enzymes to normalcy by the antioxidative action of its bioactive constituents.

Conflict of interest statement

We declare that we have no conflict of interest.

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