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Protective effects of *Cyathula prostrata* leaf extract on olanzapine-induced obese rats

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ABSTRACT

Olanzapine, an atypical antipsychotic drug often induces excessive weight resulting in obesity. The adverse effect hinder adherence to drug regimens and therefore relapse into psychosis. Traditionally in Nigeria, leaf broth from *Cyathula prostrata* leaf is consumed to achieve weight loss. Rats were first administered 50-200 mg/kg bw CPLE and orlistat (5 mg/kg bw), used as reference. Rats were then administered 8 mg/kg bw of olanzapine one hour after the administration of the CPLE and orlistat, all the administration were done for 28 days. Those with body mass index (BMI) > 0.5 g/cm^2 were considered obese. The influence of the extract at varying doses on BMI, lipid profiles, oxidative and enzyme markers in the heart and liver of the obese rats were evaluated. Anthropometric data showed that CPLE significantly ($p < 0.05$) induced weight loss and attenuated BMI increase when compared to un-treated olanzapine-induced obese rats. Biochemical analyses also revealed reduction in the serum level of LDL-c, total cholesterol, triglycerides, lipase and creatine kinase activities in CPLE-treated groups. Concentration of malondialdehyde was decreased, while the activities of antioxidant enzymes as well as that of alkaline phosphatase, alanine and aspartate aminotransferase were increased following administration of CPLE to the obese rats. Findings from this study supported the indigenous use of extracts from *C. prostrata* leaf in the management of obesity. The study concluded that CPLE can protect against weight gain, obesity, dyslipidaemia, oxidative stress and alteration in the heart and liver function parameters induced by olanzapine co-administration in rats.

Keywords: BMI, obesity, olanzapine, orlistat.

INTRODUCTION

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems [1]. A person with a BMI of 30 or more is generally considered obese [1, 2]. Body mass index is an index of weight for height which is used to classify overweight and obesity. A BMI greater or equal to 25 kg/m^2 is overweight while a BMI greater or equal to 30 kg/m^2 is obesity [1, 2]. Worldwide, obesity occur as a result of an increase intake of energy dense foods that are high in sugar, fat and salt but low in vitamins, minerals as well as other required micronutrients and a reduction in physical activity [1]. Apart from these factors, drugs particularly antipsychotic drugs such as olanzapine, quietapine, ziprazidone, sulpiride and risparidone which are used for treating psychotic conditions also contribute to the aetiology of obesity [3]. Obesity affects every part of the body including every organ there in from the head to the toe; this is why an obese individual is susceptible to a range of other diseases including diabetes mellitus, cardiovascular diseases, infertility, respiratory anomalies, non-alcoholic fatty liver diseases, cancer and so on [4].

The prevalence of obesity is increasing worldwide representing a primary health concern as a result of the relationship between obesity and a number of other chronic diseases. In 2016, globally, more than 1.9 billion adults were overweight of which more than 650 million are obese, 41 million children under the age of five were overweight or obese and 34 million children and adolescent were overweight or obese [2]. In developed countries like USA, Australia and Canada it is increasing at a faster rate [5]. It has also been assumed to be an important cause of human deaths [6]. In the European Union, half population of adults and approximate 20% of school-age children are reported as obese, while in England over a quarter of adults (26%) were reported as obese in 2010 [5]. The scourge of obesity is not restricted to developed societies alone, almost all countries are facing obesity endemic, in developing countries, obesity becomes the most glaring outward sign of the changing face of malnutrition, the problem of obesity is increasing in developing countries, it is estimated that over 775 million people suffer from obesity related problems [7, 8]. Obesity contributes about 2.8 million deaths each year, risk of heart diseases, strokes and diabetes increase steadily with increasing body mass index [8]. The disorders as a result of obesity will be number one causes of death among needy population by the year 2030 [2]. The trend is almost the same in the developing countries of the world. In Indonesia and china,

the incidence of obesity has doubled, while in Congo, it is six times higher [2]. In the past 36 years the prevalence of obesity has jumped to about 1400% in Burkina Faso and more than 500% in Benin, Ethiopia, Ghana and Togo [2]. In Nigeria, about 35% of the population are overweight and not more than 5% are wealthy, so about 30% of poor Nigerians are already suffering from overweight [9]. Obesity can be treated by measures which include dietary changes, physical exercises, behaviour changes, weight reduction medication as well as weight reduction surgery. The preferred treatment for obesity is dieting and physical exercise, however due to busy schedules and sedentary lifestyle, these two methods are not practicable on a regular basis. Weight reduction surgery also runs out of the options due to the exorbitant cost involved. Hence the use of drugs remains the better option for the treatment of obesity. These drugs alter one of the fundamental process in the human body, and these include suppression of appetite, alteration in the metabolism or absorption of calories. Many drugs have been used over the year to prevent and manage obesity. However despite the increase in the prevalence of this disease and promising results of some of these drugs, most of the drugs that have been approved and marketed as antiobesity drugs have been withdrawn from the market due to serious side effects [10]. For example in the year 2000 phentermine, an appetite-suppressant drug belonging to the family of β-phenethylamine was withdrawn by the European Medicines Agency (EMA) due to higher risk to benefit ratio [10]. In the same year 2000 mazindol and diethylpropion were also withdrawn. Rimonabant is another appetite-suppressant which was available for use in 2006 but was never approved by the Food and Drug Administration (FDA), its use was also later suspended by EMA in 2008 due to increased risk of psychiatric side effects such as anxiety, suicidal, sleep disorder and depression. Sibutramine is also an appetite-suppressant which is a selective noradrenaline/serotonin reuptake inhibitor, it was widely used after its approval by the FDA in 1997, and however in 2010 it was withdrawn by the same FDA due to increased risk of serious nonfatal cardiovascular events like stroke and myocardial infarction (Kang and Park, 2012). Orlistat is one of the few antiobesity drugs approved by the FDA and available for long-term treatment of obesity. Orlistat is a lipase inhibitor; it can inhibit gastrointestinal and pancreatic lipases. By inhibiting lipases, orlistat prevents the hydrolysis of triacylglycerol into free fatty acid and glycerol thereby reducing the absorption of dietary fat by about 30% [10]. Despite the promising results of orlistat for the treatment of obesity it is associated with undesirable side effects which include flatulence, liquid stool, diarrheoa, fecal urgency, abdominal cramping, liver problem, elevations, in liver transaminases, alkaline phosphatase, hepatitis and so on [11]. Due to all these side effects orlistat may not be well tolerated. Hence it is crucial to discover an alternative therapy with little or no side effects from plants. A large number of plants are known to possess weight reducing effects; these plants are cheaper, locally available, and easily consumable and have little or no adverse effects. Despite the use of these plants in traditional medicine, majority are so far not scientifically evaluated [5]. *Cyathula prostrata* is one of such plants that are used traditionally to achieve weight reduction, it belongs to the family of Amarantacae, it grows in moist ecologies, it is known as *Sawere pepe* in Yoruba, *Dakandafi* in Hausa and *Agbirigba* in Igbo. There are no scientific reports to authenticate or refute the acclaimed weight reducing potential of Cyathula *prostrate*, hence the need for this study.

MATERIALS AND METHODS

Plant Material

Fresh leaves of *Cyathula prostrata* were obtained from a farm land in Iloffa, Oke Ero Local Government Area, Kwara State, Nigeria in July 2015. The authentification of the plants was done at the Plant Biology Department of the University of Ilorin, Ilorin Kwara state, Nigeria. A voucher specimen was deposited at the Herbarium of the Department and a voucher number was issued.

Experimental Animals

Female Wistar rats weighing between 100-130g were used for the study. The animals were obtained from the Animals Holding Unit of the Department of Biochemistry, University of Ilorin. They were housed in plastic cages at room temperature and were allowed to acclimatize for one week; with free access to water and normal rat pellet *ad libitum.* Ethical clearance for the study was obtained from the University of Ilorin Ethical Review Committee where ethical number was issued.

Chemicals and Reagents

All chemicals used were of analytical grade and all Kits for enzymes (alanine transaminase, aspartate transaminase, alkaline phosphatase, Lipase and creatine kinase), lipid profiles (total cholesterol, triglycerides, HDL-c) used were products of Randox Laboratories Limited, UK. Orlistat was obtained from Micro Labs Limited, India, olanzapine was obtained from John lee Pharmaceutical Limited, Mumbai.

METHODS

Preparation of Drugs

Olanzapine (100 mg) was dissolved in 1 ml of glacial acetic acid and made up to 10 ml with distilled water; the pH was adjusted to 7.0 with 0.1 M NaOH. Orlistat (250 mg) was dissolved in 50 ml 80% ethanol and centrifuge at 4,000 g for 5 minutes, the supernatant obtained was used.

Preparation of Plant Extract

Fresh leaves of *Cyathula prostrata* were rinsed twice with tap water and then dried at room temperature for 7 days. The dried leaves were then grounded into powder using an electric blender. The dried powder of the plant (250 g) was then extracted in 1000 ml 80% ethanol for 48 hours. The extract was filtered through Whatman No. 1 filter paper. The resulting filtrate was then evaporated under reduced pressure using a rotary evaporator at 40ºC to give a percentage yield of 16.55 ± 2.15% (w/w) *Cyathula prostrata* Leaf extract (CPLE). The residue was then reconstituted in distilled water to give the required doses used.

Qualitative and Quantitative Determination of Secondary Metabolites in *Cyathula prostrata* leaf Extract

Total Phenolic

Phenols were determined using the method of [12]. Solution of $FeCl_3$ (2 ml of 2%) was mixed with 1.o g of the extract, the mixture turned black and this indicated the presence of phenols. Total phenolic content of the extract was then estimated according to the method of [13]. The extract (0.2 g)) was dissolved in 2.5 ml of distilled water, 100 µl of the mixture was taken into a test tube and made up to the volume of 1ml with distilled water. Folin-Ciocalteu reagent (500 µl), 400 µl sodium carbonate solution and 2.5 ml distilled water were added sequentially to the test tube. The mixture was left at room temperature

for 40 minutes. And the absorbance was taken at 760 nm against the reagent blank. The analysis was performed in triplicates and the results were expressed as garlic equivalent per gram of dry weight.

Total Flavonoids

Flavonoids were determined using the procedure described by [12]. The extract (0.2 g) was dissolved in 2.5 ml of distilled water, 1.0 ml of the solution was treated with dilute NaOH, followed by the addition with 2 ml of dilute HCl. A yellow precipitate was observed this indicated the presence of flavonoids. Total flavonoids content was then determined by using the methods described by [14]. The extract (0.2 g) was dissolved in 2.5 ml of distilled water, 1 ml of the extracts solution or standard solution of quarcetin (500 ug/ml) was added to 10 ml volumetric flask containing 4 ml of distilled water. $NaNO_2$ (0.3 ml of 5%) was added to the mixture. After 5 minutes, 0.3 ml of 10% $AlCl_3$ was added. At 6th min, 2 ml of 1M NaOH was added and the total volume was made up to 10ml with distilled water. The solution was mixed thoroughly and the absorbance was taken against prepared reagent blank at 510 nm. Total flavonoid content of the extract was expressed as percentage of quarcetin equivalent per 100 mg of dry weight.

Total Alkaloids

The presence of alkaloids was determined using the procedure described by [14] with a slight modification. The extract (0.2 g) was weighed and defatted with 2 ml of 5% ethyl ether for 10 minutes. The defatted sample was extracted for 10 minutes with 5.0 ml of aqueous HCl on a steam bath. The resulting mixture was centrifuged for 10 minutes at 3000 rpm to remove filtrate. The filtrate (2 ml) was treated with a few drops of Wagner‘s reagent. Brownish red precipitate was observed this indicated the presence of alkaloids. Total alkaloids were also determined using the methods described by [15]. The extract (0.5 g) was weigh into a 250 ml beaker and 20 ml of 10% acetic acid in ethanol was added and covered and allowed to stand at room temperature for 2 hours. The mixture was filtered and the extract was concentrated on a water bath. Concentrated Ammonium hydroxide was added to the mixture (drop wise) until completion of the precipitation. The whole solution was allowed to settle and the precipitate was collected and washed with dilute ammonium hydroxide and then filtered. The residue was the alkaloid, which was dried and weigh.

Total Tannins

Tannins were determined using the procedure described by [16]. The extract (0.5 g) was stirred with 5.0 ml of distilled water. The mixture was then filtered and drops of ferric chloride reagent was added to the filtrate. A blue-black precipitate was observed this indicated the presence of tannins. Total tannins were also determined using the method [16]. The extract (0.2 g) was weighed into 80 ml conical flask, 5 ml of distilled water was added and shaken for 1 hour using a mechanical shaker. The mixture was filtered and made to 10 ml with distilled water. The filtrate (5 ml) was pipetted out into a test tube and mixed with 2ml of 0.1M $FeCl_3$ in 0.1M NH_4Cl and 0.008M potassium ferrocyanide. The absorbance was taken at 320 nm within 10 minutes. Total tannins were calculated from the absorbance values.

Total tannins = change in absorbance of sample x 100 mg

Total Saponins

Saponins were determined using the procedure described by [15]. The extract (0.2 g) was shaken with water in a test tube, frothing which persist on warming was observed this indicated the presence of saponins. The method of [17]. was then used for the determination of total saponins. Finely ground dried powder of the plant (1.0 g) was weighed into a 250 ml beaker and 100 ml of isobutyl alcohol was added. The mixture was shaken on a mechanical shaker for 5 hours to ensure uniform mixing. Thereafter, the mixture was filtered through a whatman no. 1 filter paper into a 100 ml beaker containing 20 ml of 40% saturated solution of $MgCO_3$. The resulting mixture was again filtered to obtain a clear colourless solution. The colourless filtrate (1 ml) was pipetted into a 50 ml volumetric flask and 2 ml of 5% $FeCl_3$ solution was added and made up to the marked level with distilled water. This was then allowed to stand for 30 minutes for a blood red colour to develop. Saponins standard (1-10 ppm) was prepared from saponins stock solution. The standard solutions were treated similarly with 2 ml of 5% $Fecl_3$ solution as earlier described. The absorbance of the samples as well as standard saponins solutions were read after colour development at a wavelength of 380 nm.

Total saponins (mg) was calculated as:

$$\frac{\text{change in absorbance of sample}}{\text{change in absorbance of standard}} \times \text{concentration of standard}$$

Total Glycosides

Glycosides were determined using Kella-Killiani test as described by [18]. The extract (0.2 g) was dissolved in 2.0 ml of glacial acetic acid containing one drop of ferric chloride solution. This was then under laid with 1.0 ml of concentrated H_2SO_4 a brown ring was observed at the interface this indicated the presence of glycosides. Total glycosides were determined using the procedure described by [18]. The extract (2.0 g) was dissolved in 20 ml of distilled water, 10 ml of the extract solution was pipetted into a 250 ml conical flask, and 50 ml chloroform was added and shaken on a mechanical shaker for 1 hour. The mixture was filtered into a conical flask. Ten ml of pyridine and 2 ml of 2% sodium nitroprusside were added and shaken thoroughly for 10 minutes. NaOH (3 ml of 20%) was later added to develop a brownish yellow colour. The series of standard of concentration ranging from 0.5 mg/ml prepared from 1000 mg/ml were treated similarly like the extract, the absorbance of the extract as well as standards were read at a wavelength of 510 nm.

Total glycosides (mg) =

$$\frac{\text{change in absorbance of sample}}{\text{change in absorbance of standard}} \times \text{concentration of standard}$$

Induction of Obesity

The rats (30) were divided into 6 groups (A-F) of 5 animals per group. Distilled water (0.2 ml) was administered to the animals in group A while all the animals in groups B-F were administered 0.2 ml olanzapine (8 mg/kg BW). In addition, one hour before the administration of olanzapine animals in group C were administered 0.2 ml orlistat (5 mg/kg BW) while animals in groups D-F were administered 0.2 ml CPLE (50 mg/kg BW, 100 mg/kg BW and 200 mg/kg BW) respectively, All the administration was done orally for 28 days. Animals with BMI greater than 0.5 g/cm^2 at the end of 28 days were considered obese [18].

Determination of Feed intake

Feed intake of the rats was determined by measuring the amount of

feed giving to the animals in the morning using a weighing balance. Feed intake was then calculated by subtracting the amount of food left over in each group from the measured amount of food provided at the previous day (gm/day/group). The mean of food intake was represented in g/week/group.

Anthropometrical Determinations

The body weight of the animals were measured weekly in grams (g). The body length (nose-to-anus length) were determined weekly in centimeter (cm) in all the animals. The body weight and body length were used to determine the body mass index (BMI) as described by [19].

Biochemical Analysis

Total cholesterol was determined using the method described by [20] Triacylglycerol was determined using the method described by [21]. High density lipoprotein cholesterol was determined using the method of [22]. Low density lipoprotein was determined using the method described by [23]. Atherogenic indices were Atherogenic index (AI) was determined as total cholesterol/HDL-c as described by [24]. Castelli risk index I (CRI) was determined as TG/HDL-c, Castelli risk index II (CRII) was determiner as LDL–c/HDL-c as described by [25]. Creatine kinase (CK) activity was assayed for using the method described by [26]. In vivo pancreatic Lipase activity was assayed for using the method of [27]. Leptin concentration was determined using a solid phase enzyme-linked immunosorbent assay (ELISA). Lipid peroxidation was determined using the method of [28]. Superoxide dismutase activity was assayed for using the method described by [29]. Catalase activity was assayed for using the procedure described by [30]. with slight modification. Glutathione peroxidase activity was assayed for using the method described by [31]. Glutathione reductase activity was assayed for using the method described by [32]. Alanine aminotransferase (ALT) activity was assayed for using the method described by [33]. Alkaline phosphatase (ALP) was assayed using the method described by [34]. Protein concentration was determined using Biuret reagent as described by [35].

Statistical Analysis of Data

All results were expressed as mean ± Standard Error of Mean (SEM). One way analysis of variance (ANOVA) using graph pad prism (version 7) followed by Tukey's Multiple Comparisons Test to analyse differences among different mean, differences were considered statistically significant at $p < 0.05$.

RESULTS

Secondary Metabolites in *Cyathula prostrata* Leaf Extract

The secondary metabolites detected in *C, prostrata* Leaf extract (CPLE) are presented in Table 1. The extract was found to contain 6 secondary metabolites namely: alkaloids, saponins, tannins, phenols, flavonoids and glycosides. Phenols were found to be the most abundant in the extract constituting about 43.69% while glycosides were found to be the least constituting about 1.85%.

Table 1: Secondary Metabolites Detected in C. *prostrata* Leaf Extract

Secondary metabolites	Quantity (mg/g)
Alkaloids	59.15 ± 0.88
Saponins	144.36 ± 2.32
Tannins	71.93 ± 0.71
Phenols	343.33 ± 3.71
Flavonnoids	152.56 ± 2.32
Glycosides	14.54 ± 0.34

Feed Intake of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Feed intake of obese rats pre-treated with CPLE are shown in Table 4.3. Treatment with olanzapine resulted in significant ($p < 0.05$) increase in feed intake when compared with the control, and animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Significant ($p < 0.05$) increase in feed intake was observed in control when compared with the animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. No significant ($p < 0.05$) difference in feed intake was observed in animals pre-treated with orlistat when compared with all the investigated doses of the extract.

Table 2: Feed Intake (g) of Obese Rats Pre-treated with *Cyathula prostrate* Leaf Extract for 28 Days

Day	Control (normal rats)	Obese- untreated	Obese + orlistat	Obese + 50 mg/kg BW CPLE	Obese+ 100 mg/kg BW CPLE	Obese + 200 mg/kg BW CPLE
0	93.20 ± 4.85^a	96.10 ± 1.58^a	94.24 ± 2.49^a	94.20 ± 2.91^a	95.60 ± 3.78^a	95.20 ± 2.49^a
7	96.40 ± 4.56^a	108.20 ± 4.17^b	95.84 ± 1.79^c	96.60 ± 3.21^a	96.60 ± 4.21^a	94.20 ± 3.11^d
14	100.20 ± 1.48^a	112.40 ± 5. 62^b	96.44 ± 2.07^c	97.80 ± 2.49^c	97.80 ± 3.35^c	96.20 ± 2.49^c
21	107.40 ± 2.07^a	113.40 ± 0.10^b	104.64 ± 1.07^c	100.30 ± 3.46^c	101.60 ± 4.21^c	100.30 ± 3.46^c
28	107.20 ± 4.18^a	115.24 ± 2.21^b	107.24 ± 2.77^c	106.80 ± 2.59^c	105.20 ± 2.74^c	106.40 ± 2.88^c

Values are means ± SEM of five replicates; values with different superscripts across the rows indicate significance at $p < 0.05$
CPLE= *C. prostrata* Leaf Extract

Body weight of obese rats pre-treated with *Cyathula prostrata* Leaf Extract for 28 days

Body weight of obese rats pre-treated with *Cyathula* prostrata leaf extract (CPLE) are shown in Figure 1. Significant ($p < 0.05$) increase in body weight was observed in obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Body weight of animals pre-treated with orlistat compared favorably with the control up to day 14. However from day 14 onward pre-treatment with orlistat significant ($p < 0.05$) decreased body weight when compared with the control and all the investigated doses. Body weight of animals pre-treated with 100 and 200 mg/kg BW CPLE significantly ($p < 0.05$) decreased when compared with the control.

Body Mass Index of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Body mass index (BMI) of obese rats pre-treated with *Cyathula prostrata* leaf extract CPLE are shown in Figure 2. Significant ($p < 0.05$) increase in BMI was observed in obese-untreated rats when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Animals pre-treated with orlistat showed no significant ($p < 0.05$) difference in BMI when compared with the control up to day 14. However from day 14 onward pre-treatment with orlistat significantly decrease BMI when compared with the control and all the investigated doses of CPLE. Body mass index of animals pre-treated with 100 mg/kg BW CPLE showed no significant ($p<0.05$) difference when compared with animals pre-treated with orlistat and significantly ($p<0.05$) decreased when compared with the control.

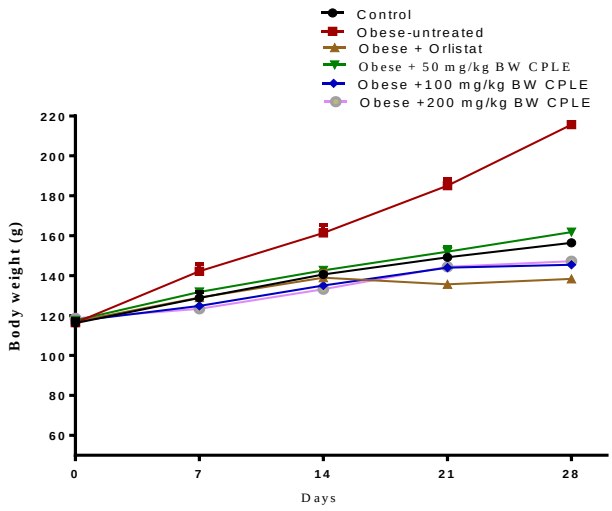

Figure 1: Body Weight of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Values are means ± SEM of five replicates; different point values indicated significance at $p < 0.05$.

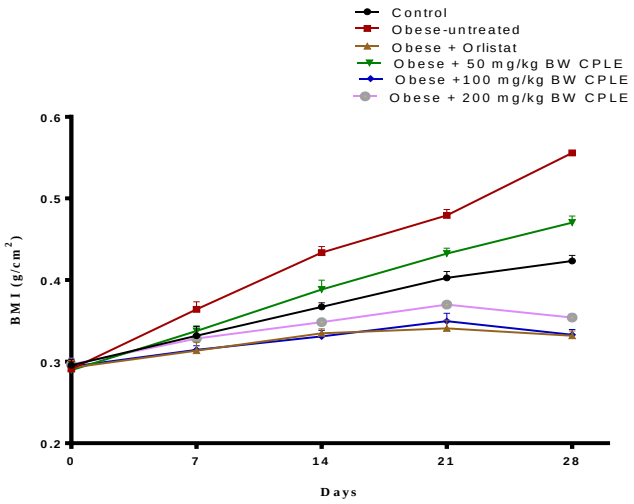

Figure 2: Body Mass Index of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Values are means ± SEM of five replicates; different point values indicated significance at $p < 0.05$.

Total Cholesterol and Triglycerides Concentrations in the Serum of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Total cholesterol and triglycerides of obese rats pre-treated with *Cyathula prostrata* leaf extract (CPLE) are presented in Figure 3. Significant ($p < 0.05$) increase in total cholesterol and triglycerides were observed in obese-untreated animals when compared with the control, animals pre-treated with orlistat and all the investigated doses of CPLE. There was no significant ($p < 0.05$) difference in total cholesterol of the control when compared with the animals pre-treated with 100 and 200 mg/kg BW CPLE. There was no significant ($p < 0.05$) difference in triglycerides concentration of the control when compared with the animals pre-treated with orlistat and 50 mg/kg BW CPLE. Animals pre-treated with 100 and 200 mg/kg BW CPLE showed significant ($p < 0.05$) decrease in triglycerides concentration when compared with the control.

High Density Lipoprotein Cholesterol (HDL-C) and Low Density Lipoprotein Cholesterol (LDL-C) Concentrations in the Serum of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

High density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) of obese rats pre-treated with CPLE are shown in Figure 4.4. Significant ($p < 0.05$) decrease in HDL-C and significant ($p < 0.05$) increase in LDL-C were observed in obese-untreated animals when compared with the control, animals pre-treated with orlistat and all the investigated doses of CPLE. There was no significant ($p < 0.05$) difference in HDL-C and LDL-C of the control when compared with the animals pre-treated with 100 and 200 mg/kg BW CPLE. Animals pre-treated with 100 and 200 mg/kg BW CPLE exhibited significant ($p < 0.05$) increase in HDL-C and significant ($p < 0.05$) decrease in LDL-C when compared with animals pre-treated with orlistat.

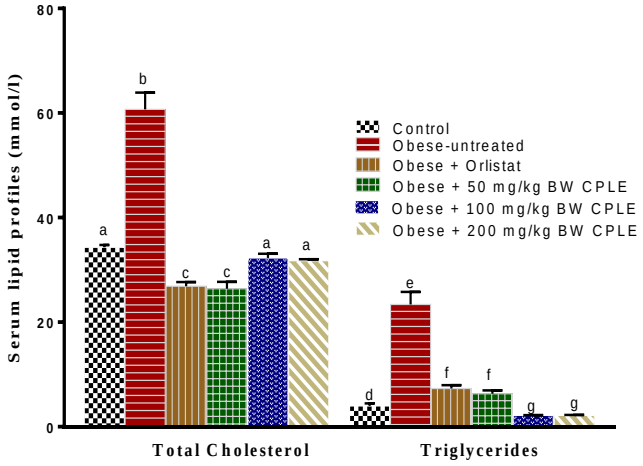

Figure 3: Total Cholesterol and Triglycerides Concentrations of Obese Rats Pre-treated with CPLE for 28 Days

Values are means ± SEM of five replicates; bars with superscripts indicate significance at $p < 0.05$. CPLE= *C. prostrata* leaf extract

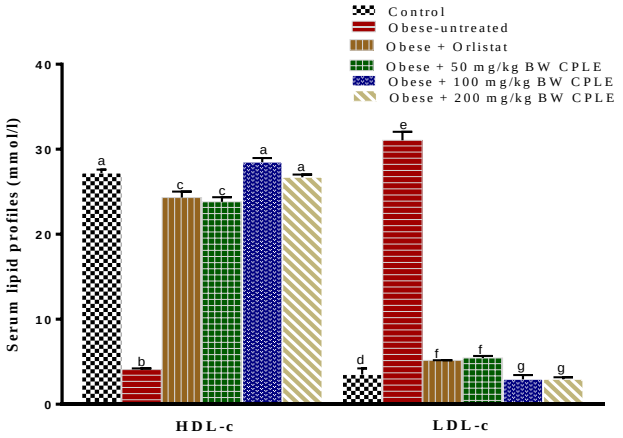

Figure 4: High Density Lipoprotein Cholesterol (HDL-C) and Low Density Lipoprotein Cholesterol (LDL-C) Concentrations in the Serum of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days.

Values are means ± SEM of five replicates; bars with superscripts indicate significance at $p < 0.05$. CPLE=*C. prostrata* Leaf Extract.

Atherogenic Indices of Obese Rat Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Atherogenic indices of obese rats pre-treated with CPLE are presented in Table 4.4. Significant ($p < 0.05$) increase in all the atherogenic indices was observed in obese-untreated animals when compared with the control, animals pre-treated with orlistat and all the investigated doses of CPLE. There was no significant ($p < 0.05$) difference in all the atherogenic indices of the control when compared with the animals pre-treated with orlistat and all the investigated doses of CPLE.

Table 3: Atherogenic Indices of Obese rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Test Groups	AI	CRI	CRII
Control	0.02 ± 0.002 [a]	1.26 ± 0.030 [a]	0.13 ± 0.020 [a]
Obese-untreated	0.57 ± 0.050 [b]	14.86 ± 0.660 [b]	7.61 ± 0.230 [b]
Obese + Orlistat	0.02 ± 0.010 [a]	1.26 ± 0.030 [a]	± 0.010 [c]
Obese + 50 mg/kg BW CPLE	0.01 ± 0.001 [a]	1.41 ± 0.050 [c]	0.23 ± 0.020 [c]
Obese + 100 mg/kg BW CPLE	0.01 ± 0.001 [a]	1.24 ± 0.010 [a]	± 0.010 [a]
Obese + 200 mg/kg BW CPLE	0.01± 0.001 [a]	1.19 ± 0.020 [a]	0.11 ± 0.010 [a]

Values are means ± SEM of five replicates; values with different superscripts down the column indicate significance at $p < 0.05$; AI = Atherogenic index; CRI = Castelli risk Index-I CRII= Castelli risk index-II; CPLE=*C. Prostrata* Leaf Extract

Creatine Kinase Activity in the Serum of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Creatine kinase activity of obese rats pre-treated with CPLE are shown in Figure 5. Significant ($p < 0.05$) increase in creatine kinase activity was observed in obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Animals pre-treated with 100 and 200 mg/kg BW CPLE showed significant ($p < 0.05$) decrease in creatine kinase activity when compared with the control and the animals pre-treated with orlistat.

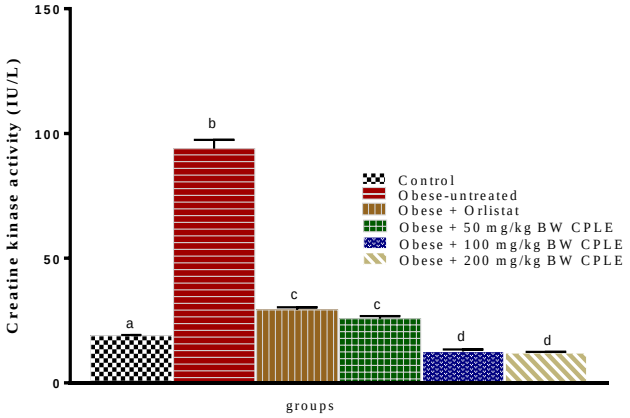

Figure 5: Creatine Kinase Activity in the Serum of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Values are means ± SEM of five replicates; bars with different superscripts indicate significance at $p < 0.05$; CPLE = *C. prostrata* Leaf Extract

Pancreatic Lipase Activity of obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Pancreatic lipase activity of obese rats pre-treated with CPLE are shown in Figure 6. Significant ($p < 0.05$) increase in lipase activity was observed in obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Pancreatic lipase activity of animals pre-treated with 100 and 200 mg/kg BW significantly ($p < 0.05$) decrease when compared with the control and the animals pre-treated with orlistat.

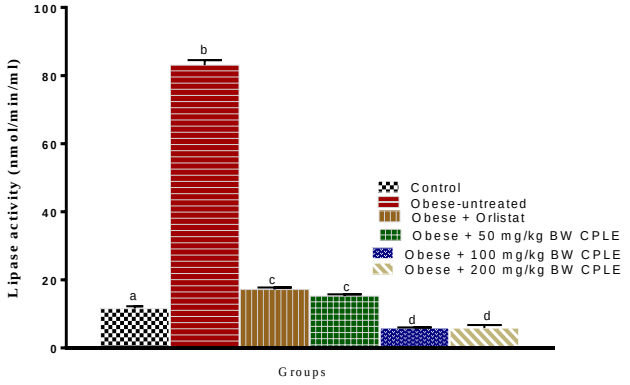

Figure 6: Pancreatic Lipase Activity of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Values are means ± SEM of five replicates; bars with different superscripts indicate significance at $p < 0.05$; CPLE=*C. prostrata* Leaf extract

Malondialdehyde Concentration in the Liver and Heart of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Malondialdehyde (MDA) concentration in the liver and heart of obese rats pre-treated with CPLE are shown in Figure 7. Significant ($p < 0.05$) increase in MDA concentration of both the liver and the heart was observed in obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. No significant ($p < 0.05$) difference was observed

in MDA concentration of the control in both the liver and the heart when compared with the animals pre-treated with 100 and 200 mg/kg BW CPLE. Animals pre-treated with 100 and 200 mg/kg BW exhibited significant ($p < 0.05$) decrease in malondialdehyde concentration when compared with the animals pre-treated with orlistat.

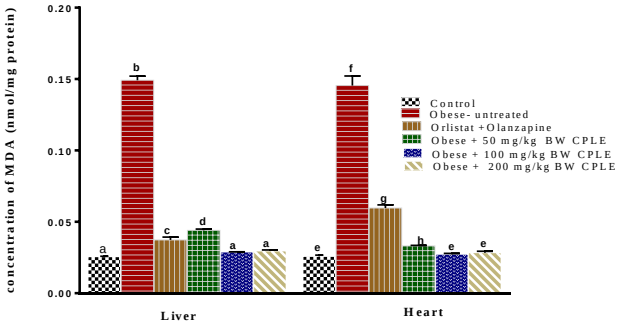

Figure 7: Malondialdehyde Concentrations in the Liver and the Heart of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Values are means ± SEM of five replicates; bars with different superscript indicate significance at $p < 0.05$; CPLE= *C. prostrata* Leaf extract

Antioxidant Enzymes Activities in the Liver of Obese rats Pre-treated with CPLE for 28 Days

Antioxidant enzymes activities in the liver of obese rats pre-treated with CPLE are shown in Table 4. Significant ($p < 0.05$) decrease was observed in the activity of all the antioxidant enzymes investigated in the liver of obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Animals pre-treated with 100 mg/kg BW CPLE showed significant ($p < 0.05$) increase in the activity of all the antioxidant enzymes investigated when compared with the control and animals pre-treated with orlistat and other investigated doses of CPLE.

Table 4: Antioxidant Enzymes Activities in the Liver of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Group	Catalase (nmol/min/mg protein)	SOD (nmol/min/mg protein)	GR (nmol/min/mg protein)	GPx (nmol/min/mg protein)
Control	305.92 ± 6.44^a	455.63 ±7.09^a	2.94 ± 0.45^a	23.46 ± 3.45^a
Obese-untreated	12.31 ± 1.0^b	77.77 ±3.56^b	0.39 ± 0.11^b	7.35 ± 0.23^b
Obese + Orlistat	239.47 ± 4.10^c	262.13 ±3.14^c	3.07 ± 0.17^c	10.22 ± 0.10^c
Obese + 50 mg/kg BW CPLE	214.76 ± 8.59^d	358.45 ± 3.72^d	2.35 ± 0.01^d	20.35 ± 0.01^d
Obese + 100 mg/kg BW CPLE	359.25 ± 2.44^e	480.44 ± 1.11^e	3.07 ± 0.10^c	25.74 ± 0.65^e
Obese + 200 mg/kg BW CPLE	256.55 ± 1.92^f	356.55 ± 1.92^d	2.35 ± 0.11^d	21.34 ± 0.25^d

Values are means ± SEM of five replicates; values with different superscripts down the column indicate significance at $p < 0.05$
SOD = Superoxide Dismutase; GR = Glutathione Reductase; GPx = Glutathione Peroxidase CPLE=*C. Prostrata* Leaf Extract

Antioxidant Enzymes Activities in the Heart of Obese Rats Pre-treated with CPLE for 28 Days

Antioxidant enzymes activities in the heart of obese rats pre-treated with CPLE are shown in Table 5. Significant ($p < 0.05$) decrease was observed in the activity of all the antioxidant enzymes investigated in the liver of obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Animals pre-treated with 100 mg/kg BW CPLE showed significant ($p < 0.05$) increase in the activity of all the antioxidant enzymes investigated in the heart when compared with the control and animals pre-treated with orlistat and other investigated doses of CPLE.

Table 5: Antioxidant Enzymes Activities in the Heart of obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 days

Group	Catalase (nmol/min/mg protein)	SOD (nmol/min/mg protein)	GR (nmol/min/mg protein)	GPx (nmol/min/mg protein)
Control	514.63± 10.65^a	335.84 ± 7.09 ^{a}	2.36 ± 0.11^a	57.35 ± 6.68^a
Obese-untreated	158.46 ± 0.65^b	26.26 ± 0.42^b	0.92 ± 0.07^b	30.95 ± 1.10^b
Obese + Orlistat	212.46 ± 0.98^c	145.26 ± 1.19^c	0.82 ± 0.46^c	41.14 ± 1.53^c
Obese + 50mg/kg BW CPLE	410.95 ± 0.88^d	245.80 ± 1.21^d	1.85 ± 0.07^d	41.36 ± 1.20^c
Obese + 100mg/kg BW CPLE	559.25 ± 2.44^e	448.14 ± 2.01^e	3.02 ± 0.34^e	67.56 ± 6.68^d
Obese + 200mg/kg BW CPLE	385.84 ±1.92^f	256.65 ± 1.07^f	1.76 ± 0.23^d	45.28 ± 1.03^c

Values are means ± SEM of five replicates; values with different superscripts down the column indicate significance at $p < 0.05$
SOD = Superoxide Dismutase; GR = Glutathione Reductase; GPx = Glutathione Peroxidase; CPLE= *C. Prostrata* Leaf extract

Alkaline Phosphatase Activity in the Serum, Liver and Heart of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Alkaline phosphatase (ALP) activity in the serum, liver and heart of obese rats pre-treated with CPLE are shown in Table 6. Significant ($p < 0.05$) increase in the activity of serum ALP and significant ($p < 0.05$) decrease was observed in the liver and the heart of obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE respectively. Pre-treatment with 100 mg/kg BW CPLE significantly ($p < 0.05$) increase the activity of ALP in the liver and the heart and significantly ($p < 0.05$) decrease the activity in the serum when compared with the control and the animals pre-treated with orlistat and other investigated doses of CPLE.

Table 6: Alkaline Phosphatase (nM/min/mg protein) Activity in the Serum, liver and Heart of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

Group	Liver	Heart	Serum
Control	187.90 ± 09.60[a]	130.20 ± 10.95[a]	22.75 ± 02.15[a]
Obese-untreated	83.08 ± 00.84[b]	20.52 ± 00.72[b]	52.53 ± 00.09[b]
Obese + Orlistat	118.90 ± 00.88[c]	82.90 ± 00.66[c]	27.79 ± 10.65[c]
Obese + 50 mg/kg BW CPLE	134.60 ± 04.44[d]	90.34 ± 02.32[d]	24.80 ± 00.12[d]
Obese + 100 mg/kg BW CPLE	195.70 ± 00.36[e]	141.20 ± 01.41[e]	21.18 ± 00.24[e]
Obese + 200 mg/kg BW CPLE	131.70 ± 06.60[d]	64.33 ± 00.66[f]	26.48 ± 05.27[f]

Values are means ± SEM of five replicates; values with different superscripts down the column indicates significance at $p < 0.05$
CPLE= *C. Prostrata* Leaf extract

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities in the serum and tissues of obese rats CPLE for 28 days

Alanine Aminotransferase and Aspartate Aminotransferase activities in the serum and tissues of obese rats pre-treated with CPLE are shown in Table 4.8. Significant ($p < 0.05$) increase in the activity of serum ALT and AST and significant ($p < 0.05$) decrease was observed in the liver and heart of obese-untreated animals when compared with the control, animals pre-treated with orlistat, 50, 100 and 200 mg/kg BW CPLE. Animals pre-treated with 100 mg/kg BW CPLE showed significant ($p < 0.05$) increase in the activity of ALT and AST in the liver and heart and significant ($p < 0.05$) decrease in the serum when compared with the control and the animals pre-treated with orlistat and other investigated doses of CPLE.

Table 7: Alanine Aminotransferase and Aspartate Aminotransferase in the Serum, Liver and Heart of Obese Rats Pre-treated with *Cyathula prostrata* Leaf Extract for 28 Days

	ALT (IU/l)		AST (IU/l)	
Group	**Liver**	**Serum**	**Liver**	**Serum**
Control	362.55 ± 11.62[a]	15.21 ± 0.95[a]	289.94 ± 7.67[a]	21.13 ± 1.08[a]
Obese-untreated	35.22 ± 1.22[b]	45.32 ± 3.48[b]	34.38 ± 4.07[a]	239.38 ± 5.54[b]
Obese + Orlistat	163.31 ± 3.17[c]	34.45 ± 1.45[c]	134.13 ± 4.03[b]	87.51 ± 4.08[c]
Obese + 50 mg/kg BW CPLE	336.78 ± 2.58[d]	24.31 ± 0.24[d]	218.31 ± 4.06[d]	55.21 ± 4.08[d]
Obese + 100 mg/kg BW CPLE	372.55 ± 1.15[a]	15.58 ± 2.44[a]	295.31 ± 3.78[e]	20.13 ± 2.98[a]
Obese + 200 mg/kg BW CPLE	214.53 ± 5.13[e]	24.88 ± 1.56[d]	189.65 ± 2.45[c]	57.51 ± 4.08[d]

Values are means ± SEM of five replicates; values with different superscripts down the column indicate significance at $p < 0.05$; CPLE= *C. Prostrata* Leaf extract

DISCUSSION

Some of the synthetic chemical drugs that are used in the treatment of obesity have many side effects that often outweigh the benefits, thus necessitating the need to search for alternative and safe natural agents from plants [36]. *Cyathula prostrata* has been used in the traditional medicine in Africa for the treatment of different ailment which include obesity. This study aimed at exploring the potentials of *Cyathula prostrata* leaf extract in comparison with antiobesity drug orlistat, in preventing obesity.

Phytochemicals are secondary metabolites derived from plants which elicit pharmacological or toxicological effects in man and animals and play little role(s) in plant growth and development [37]. In this study, CPLE was found to contain alkaloids, tannins, saponins, phenols, flavonoids and glycosides. A synergistic relationship amongst phytochemicals in plants has been reported to be responsible for the overall medicinal effects derivable from plants [38]. These metabolites have been linked with various roles in the management of obesity and other risk factors associated with obesity. Flavonoids have been reported to have potential to decrease the accumulation of hepatic triglycerides, serum lipids, liver weight and lipid peroxidation [39]. Saponins have been reported to have energy stimulating and antihypercholesterolemic potential. It has the ability to cause a depletion in cholesterol concentration in the body by binding with cholesterol in the gut and preventing the reabsorption of cholesterol and consequently increasing the excretion of cholesterol from the body [40], thus enhancing the lipid lowering effects of the extract.

Alkaloids and flavonoids have been reported to have the ability to protect the body against oxidative stress-induced cellular damage [41]. Alkaloids and flavonoids have been reported to have the ability to decrease serum cholesterol, triglycerides, low density lipoprotein cholesterol (LDL-c), and Malondialdehyde (MDA). Alkaloids have also been reported to have the ability to increase high density lipoprotein cholesterol (HDL-c), superoxide dismutase (SOD), Catalase (CAT) levels [42, 41]. Phenols, alkaloids and flavonoids have antioxidant capability and also ability to inhibit or reduce lipase activity [43]. The non-significant change in feed intake of animals administered with CPLE when compared with the control implies that the extract was able to prevent increase in feed intake associated with olanzapine administration. The presence of secondary plant products and the bioactive constituents in *Cyathula prostrata* which are biologically important contribute to its medicinal values. The observed decrease in body weight and body mass index (BMI) with the administration of CPLE may be due to the presence of phenols, flavonoids and saponins.

Phenols and flavonoids have been reported to have lipase inhibitory effect [43]. Lipase is the enzyme that hydrolyses triglycerides into fatty acid and monoglycerols before been absorbed into the body. Inhibition or reduction of lipase activity will therefore prevent the storage of excess fat. Obesity is associated with increased serum levels of triglycerides, total cholesterol and low density lipoprotein cholesterol (LDL-c). These lipids are considered the main risk factors for dyslipidaemia and were related to accumulation of fat in the abdominal viscera [44], and are also risk factor for cardiovascular diseases [45]. Dyslipidaemia is characterized by elevated triglycerides, low concentration of High-Density Lipoprotein cholesterol (HDL-c), increased Low-density Lipoprotein cholesterol (LDL-c) and total cholesterol [45]. Studies have shown that weight gain is usually associated with increases in the concentration of lipids [45, 46]. The observed reduction in serum total cholesterol, triglycerides and LDL-c associated with increase in HDL-c in animals administered CPLE implies that the extract has beneficial effects on lipid profiles through cholesterol reducing effects. CPLE is a good source of secondary metabolites like saponins, flavonnoids and phenols that have been reported to have lipid lowering effects. Bioactive compounds such as phenols, saponins alkaloids and flavonoids have been reported to possess antioxidant and cholesterol-lowering activities [47]. Quantification of the secondary metabolites of CPLE revealed that the phenols fractions were the most abundant in CPLE, the antihyperlipidemic activity could be attributed to the presence of the phenols. The extract has antihyperlipidemic effect and this is strongly supported by the ability of the extract to attenuate the levels of LDL-c and HDL-c towards the control levels. Lowering of total cholesterol by the extract could be as a result of presence of saponins. Saponins have been reported to have the ability to bind to cholesterol thereby causing depletion of body cholesterol, preventing its reabsorption and increasing its excretion from the body [40]. Serum lipids can be divided into the proatherogenic lipoproteins and antiatherogenic HDL-c. Assessment of the relative proportions of cholesterol in these two fractions can be valuable than the individual lipid measurements. These lipids can be combined at various ratio, the combination of these lipids are powerful indicator of the risk assessment of coronary artery diseases. The higher the values, the higher the risk of developing cardiovascular diseases and *vice versa* [48]. Different combinations of these lipid profile parameters can also be used for the diagnosis and prognosis of cardiovascular disease (CVD) [49]. The different combination of the lipid profiles include atherogenic index (AI), Castelli's Risk Ratio-I (CRI) and Castelli's Risk Ratio-II (CRII). In this study high levels of AI, CRI and CRII were observed in obese-untreated animals and high levels of these indices have been reported to be associated with the risk of cardiovascular diseases [49, 50]. Low levels of AI, CRI and CRII were observed in all the animals administered with CPLE. It has been reported that lower levels of these indices are associated with lower risk of cardiovascular disease [51]. The lower levels of these indices following administration of CPLE is an indication that the extract has the ability to prevent the risk of cardiovascular diseases associated with obesity and this could be due to the presence of saponins, phenols, alkaloids and flavonoids.

Elevated activities of creatine kinase (CK) are expressed in cardiac dysfunction pathophysiology such as in myocardial and pulmonary infarction, cerebrovascular-disease and electrical shocks [52]. Obesity-induced elevated level of creatine kinase which was observed in the obese-untreated rats were significantly prevented by the administration of CPLE and the levels were within the range of values observed in the control rats implying that the extract does not pose any problem to the heart and that the extract has the ability to prevent the risk of pulmonary and myocardial infarction associated with obesity and this could be due to the presence of saponins, phenols, alkaloids and flavonoids. Pancreatic Lipase is an important enzyme in the digestion of triglycerides, it catalyses the hydrolysis of triacylglycerides into free fatty acid and monoglycerols that can easily be absorbed into the body [53]. In obesity the activity of lipase increases to be able to hydrolyse the excess triglycerides for easy absorption into the body. A greater relationship exist between lipases and serum triglycerides levels, in the sense that triacylglycerides absorption efficiency is one of the main factors contributing to the plasma triglycerides level; however, triglycerides are not absorbed as much until hydrolysed to fatty acids by lipases. The observed significant increase in lipase activity in the obese-untreated animals is an indication of increase in the concentration of triglycerides which was also observed in this study. Significant reduction ($p < 0.05$) in the activity of lipase which was observed with the administration of CPLE corresponds with decrease in the concentration of triglycerides observed with the administration of CPLE in this study. The observed significant reduction in the activity of lipase with the administration of CPLE could be attributed to the presence of phenols, flavonoids and alkaloids that have been reported to possess lipase inhibitory effects [43].

Malondialdehyde is a byproduct of lipid peroxidation in the cell. Malondialdehyde is a frequently used biomarker for lipid peroxidation. Increase in free radical generation due to oxidative stress causes over production of MDA. It readily combines with several functional groups including proteins, lipoproteins and DNA. Oxidative stress occurs when there is imbalance between production of free radicals and the ability of the body to defend or detoxify the harmful effects of free radicals. Obesity increases the mechanical and metabolic load on the myocardium, thus increasing myocardial oxygen consumption. A negative consequence of the elevated myocardial oxygen consumption is increase in the production of free radicals [54]. Significant ($p < 0.05$) increase in MDA concentration observed in the obese-untreated rats may be as a result of oxidative stress imposed on the body due to obesity and inability of the body to scavenge the free radicals produced. The observed significant ($p < 0.05$) reduction in MDA concentration in the groups administered with CPLE could be attributed to the presence of phenols, flavonoids and alkaloids that have been reported to possess powerful antioxidant activity [42, 41]. Cells of the body have a variety of defense mechanisms that intercept free radicals to prevent or limit intracellular damage and

ameliorate the harmful effects of reactive oxygen species (ROS). The defense mechanisms include the antioxidant enzymes like superoxide dismutase (SOD), Catalase (CAT), glutathione Peroxidase and glutathione reductase. Superoxide dismutase is a superoxide radical scavenging enzyme which is considered the first line of defense against the deleterious effect of free radicals in the cells. It protects tissues against free radicals by converting the superoxide radical into hydrogen peroxide and molecular oxygen (i.e. dismutation reaction), [54, 55]. Significant ($p < 0.05$) reduction in SOD activity in the liver and heart of obese-untreated rats could be as a result of increased generation of free radicals. Catalase is another potent antioxidant enzyme that catalyzes the dismutation of hydrogen peroxide, preventing damage to cell membranes and other biological structures [56]. Catalase battles against the effects of free radicals to the body by transforming harmful SOD radicals into hydrogen peroxides that later breaks down to water and oxygen molecules [57]. The activity of catalase was observed to be significantly ($p < 0.05$) reduced in the liver and heart of obese-untreated rats when compared with the control. The activity of glutathione peroxidase was also observed to decrease significantly ($p < 0.05$) in the liver and heart of obese-untreated rats when compared with the control. Glutathione peroxidase catalyses the reduction of variety of hydrogen peroxide using glutathione as a substrate, thereby protecting the cells against oxidative stress. Significant reduction in the activity of glutathione peroxidase observed in the obese-untreated rats, could be attributed to increased oxidation or decreased synthesis of glutathione. Obesity has been reported to be correlated to an increase in free radical generation as a result of oxidative stress or lipid peroxidation. The reduced activities of superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase could be as a result of continuous mopping up of free radicals. The observed significant ($p < 0.05$) increase in the activities of superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase in liver and heart of animals administered CPLE could be as a result of the extract probably inducing the synthesis of these enzymes and this could be attributed to the presence of phenols, flavonoids tannins and others that have been reported to possess antioxidant effects [42, 41].

The significant ($p < 0.05$) increase in alkaline phosphatase (ALP) activities in the serum as well as corresponding decrease in the activity of the enzyme in the liver of the obese-untreated animals might be due to disruption of membrane components or inactivation or inhibition of the enzyme *in situ*. It might also be due to reduction in the concentration of membrane bound substrates necessary for enzyme activity such as phosphate esters and phospholipids [58]. Reduction in the activity of the enzyme in tissues might affect active transport mechanisms across the plasma membrane of the cells with consequent starvation of the cells of vital molecules such as proteins or disturbance of some metabolic processes involving ALP within the cells. The observed increase in the activity of ALP in the liver as well as corresponding decrease in the activity of the enzyme in the serum of obese rats administered CPLE implies that the extract has the ability to reverse the enzyme and the integrity of the organ. Significant reduction in the activities of ALT and AST in the liver as well as corresponding increase in the activities of these enzymes in the serum of the obese-untreated animals may have resulted from leakage into the extracellular fluids occasioned by plasma membrane derangement leading to excessive leakage of cytosolic materials [59]. The increased serum ALT and AST activities could be due to obesity induced hepatolysis or leakage of the enzymes into the blood stream as a result of hepatomegaly [60, 61]. Obesity and abnormal lipid metabolism are associated with inflammation, congestion, and nonalcoholic fatty liver disease (NAFLD) leading to hepatic failure causing a boost in ALT and AST levels in the serum [62]. The observed increase in the activity of ALT and AST in the liver as well as corresponding decrease in the activity of the enzyme in the serum of obese rats administered CPLE implies that the extract has the ability to reverse the enzyme and the integrity of the organs, and also the extract did not pose any toxicity on the organ.

CONCLUSION

It can be deduced from the results of this study that CPLE is effective in preventing obesity, it is relatively safe and could be employed in producing alternative antiobesity drug. The study therefore concluded that CPLE can protect against weight gain, obesity, dyslipidaemia, oxidative stress and alterations in heart and liver function parameters induced by chronic olanzapine administration.

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Conflict of Interest

Authors declare that there is no conflict of interest.

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