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Ameliorative Effects of *Cyathula prostrata* Leaf Extract on Olanzapine-Induced Obesity in Rats

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Abstract

Obesity is a medical condition characterised by accumulation of excess body fat which may lead to reduced life expectancy and/or increased health problems. The aim of this study was to investigate the ameliorative potential of *Cyathula prostrata* ethanolic leaf extract (CPLE) on olanzapine-induced obesity in rats. The Rats were randomly distributed into 6 groups, group 1 served as the control and were administered distilled water, groups 5 - 6 were administered 8 mg/kg bw of olanzapine for 28 days to induce obesity. Rats with body mass index (BMI) > 0.5 g/cm^2 were selected, reassigned into five groups, the control remain unchanged and served as group 1, group 2 were treated with distilled water, group 3 were administered orlistat (5 mg/kg bw) and served as the reference, groups 4 - 6 were orally administered 50, 100 and 200 mg/kg bw of CPLE respectively for another 28 days. Olanzapine exposure resulted into increased in body weight, alterations in lipid profiles, elevated malondialdehyde levels as well as significant alteration ($p < 0.05$) in activities of creatine kinase, lipase and antioxidant enzymes. Treatment of the rats with CPLE significantly ($p < 0.05$) reduced weight gain as well as attenuating the olanzapine-induced alterations in lipid profiles, malondialdehyde, creatine kinase and lipase activities. Furthermore, CPLE completely reversed olanzapine-induced alterations in antioxidant enzymes activities which compared favourably with the reference drug. The study concludes that CPLE ameliorates weight gain, hyperlipidemia and oxidative stress by reducing elevated lipase activity and by restoring alterations in lipid profiles, oxidative markers, antioxidant enzymes and creatine kinase activity.

Keywords: *Ameliorative; Obesity; Olanzapine; Cyathula prostrata; Rats*

Introduction

Obesity is a medical condition which is characterised by accumulation of excess body fat which may results to reduced life expectancy and/or increased health problems [1]. 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 [2].

Worldwide, obesity occur as a result of an increase intake of energy dense foods that are high in sugar, fat, salt but low in vitamins, minerals and other required micronutrients as well as a reduction in physical activity [1]. Apart from these factors, drugs particularly antipsychotic drugs such as olanzapine, quetiapine, ziprasidone, sulpiride and risperidone which are used for treating psychotic condition

also contribute to the aetiology of obesity through appetite stimulation and reduction in physical activities [3]. Obesity diminishes every aspect of health starting from reproductive and respiratory functions to memory and mood. It also increases the risk of several chronic diseases such as diabetes, cardiovascular diseases and some cancer [4]. Obesity does this through a varieties of pathways which could be straightforward as the mechanical stress of carrying extra pounds and some involving complex changes in hormones and metabolism. The condition most strongly influenced by body weight is type 2 diabetes. Fat cells, especially those stored around the waist, secrete hormones and other substances that induces inflammation, inflammation is an essential component of the immune system and part of the healing process, however, inappropriate inflammation causes a variety of health problems. Inflammation can make the body less responsive to insulin and change the way the body metabolizes fats and carbohydrates, leading to higher blood sugar levels and, eventually, to diabetes and its many complications [1].

Body weight is directly associated with various cardiovascular risk factors. As BMI increases, so do blood pressure, low-density lipoprotein cholesterol, triglycerides, blood sugar, and inflammation. These changes translate into increased risk for coronary heart disease, stroke and cardiovascular death. Excess weight impairs respiratory function via mechanical and metabolic pathways. The accumulation of abdominal fat, for example, may limit the descent of the diaphragm, and in turn, lung expansion, while the accumulation of visceral fat can reduce the flexibility of the chest wall, sap respiratory muscle strength and narrow airways in the lungs. Cytokines generated by the low-grade inflammatory state that accompanies obesity may also impede lung function. Asthma and obstructive sleep apnea are two common respiratory diseases that have been linked with obesity [1].

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. 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 [2]. 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 been obese [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 [1,2]. Obesity contributes about 2.8 million deaths each year, risk of heart diseases, strokes and diabetes increase steadily with increasing body mass index [1]. 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 is overweight and not more than 5% are wealthy, so about 30% of poor Nigerians are already suffering from overweight [1,5]. Obesity can be treated by measures which include lifestyle changes, weight reduction medication like orlistat and Sibutramine, weight reduction surgery like gastric banding and sleeve gastrectomy. 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 [6]. Gastric banding and sleeve gastrectomy also runs out of the options due to the exorbitant cost involved. Hence the use of anti-obesity drug like orlistat remains the better option for the treatment of obesity. Despite the promising results of orlistat for the treatment of obesity, it is associated with undesirable side effects which include flatulence, diarrhea fecal urgency, abdominal cramping and liver problem [7]. Due to all these side effects, orlistat may not be well tolerated. Hence, it is crucial to explore an alternative therapy with little or no side effects from plants. A large number of plants such as *Cyathula prostrata, Capsicum annum, Lantana camara, Anthocleista vogelii, Stellaria media* and *Tinospora cordifolia* are known to have 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 the traditional medicine, majority are yet to be scientifically evaluated.

Cyathula prostrata is an annual herb found in moist ecologies; it belongs to the family of Amaranthaceae [8]. and is commonly referred to as pasture weed, pigweed and prickly chaff-flower plant. It was originally native to tropical Africa and Asia (Nigeria, Mozambique, Uganda, China, India and Vietnam) but now found growing all over the world including tropical America, Australia and the Pacific Islands [9]. It is known as *Sawere pepe* (Yoruba), *Dakan dafi* (Hausa) and *Agbirigba* (Igbo). It is used in traditional medicine for the treatment of chest troubles, constipations, scabies and for weight reduction (ethno botanical survey). Studies on extracts of *Cyathula prostrata* leaves showed good levels of flavonoids and polyphenols, as well as antioxidant, antiulcer, anti-inflammatory, antihypertensive and hepatoprotective among others [10].

In this study, the ameliorative effects of *Cyathula prostrata* leaf extract (CPLE) on olanzapine-induced obesity in female Wistar rats was investigated. More specifically, the ameliorative potential of CPLE was investigated in terms of its ability to attenuate olanzapine-induced weight gain, hyperlipidaemia and oxidative impairment.

Materials and Methods

Sample collection and extraction

Fresh leaves of *Cyathula prostrata* were obtained from a farm land in Ilofa, Oke Ero Local Government Area, Kwara State, Nigeria in July 2015. The authentication of the plants was done at the Plant Biology Department of the University of Ilorin, Ilorin Kwara state, Nigeria with voucher number UIL/001/1209. The Fresh leaves of *Cyathula prostrata* were rinsed twice with distilled water and then dried at 28ºC for 7 days. The dried leaves were then pulverised using an electric blender (Kenwood blender BL 335). The dried powder of the plant (250g) was then extracted in 1000 ml 80% ethanol for 48 hours. The extract was filtered through Whatman No. 1 filter paper, the residue was extracted twice and all filtrate were then combined and concentrated using a rotary evaporator at 40ºC. The total yield obtained (41.87g) was kept in an airtight container prior to use.

Experimental animals

Female Wistar rats weighing 110 ± 0.5g were used for the study. The animals were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin. They were housed in plastic cages at 27 ± 2ºC and were allowed to acclimatize for one week; were given water and standard rat pellets (Top Feeds Ltd, Ogorode Industrial Estate, Sapele, Delta State, Nigeria) *ad libitum.* Ethical clearance for the study was obtained from the University of Ilorin Ethical Review Committee where ethical number (UERC/ASN/2016/289) was issued.

Assay kits and drugs

Assay kits for lipase, creatine kinase, total cholesterol, triglycerides, High density lipoprotein cholesterol, were products of Randox Laboratories Limited, UK. Orlistat Olanzapine were product of Micro Labs Limited, Mumbai India, and John Lee Pharmaceutical Limited, Mumbai, India, respectively.

Experimental procedure

Animal grouping

Animals were randomly divided into 6 groups (A-F) of 7 animals per group as follow. Animals in group A were administered 0.2 ml distilled water, while all the animals in groups B to F were administered orally 0.2 ml Olanzapine (8 mg/kg BW) to induce obesity. At the end of 28 days' animals in groups B-F with BMI significantly greater than 0.5 g/cm^2 were selected and were reassigned into 5 groups (B-

F) of 5 animals per group, while animals in group A still served as the control. Distilled water (0.2 ml) was administered to the animals in groups A and B while animals in groups C-F were administered 0.2 ml orlistat, 50 mg/kg bw CPLE, 100 mg/kg bw CPLE and 200 mg/kg bw respectively for another 28 days.

Anthropometrical determinations

The body weight of the animals were determined weekly in grams (g) using a weighing balance. The body length (nose-to-anus length) were determined weekly in centimeter (cm) using a measuring tape in all the animals. The body mass index (BMI) was computed as described by Novelli., *et al*. (2007) [11].

Biochemical analysis

Total cholesterol, Triacylglycerol, High density lipoprotein cholesterol and Low density lipoprotein were determined using the method described by Fredrickson., *et al*. (1967) [12], Tietz (1990) [13], Tietz (1976) [14] and Albers., *et al.* (1978) [15] respectively. Atherogenic index, (AI), Castelli risk index were determined as described by Kuldip and Ahluwalia (2012) [16] and Castelli., *et al*. (1983) [17] respectively. Creatine kinase (CK) activity, pancreatic lipase activity and malondialdehyde were determined using the procedures described by Tietz (1986) [18], Gu., *et al*. (2011) [19] and Ohkawa., *et al.* (1979) [20] respectively. Superoxide dismutase, Catalase activity Glutathione peroxidase and Glutathione reductase activities were assayed for using the methods described by Misra and Fridovich (1972) [21], Beers and Siser (1952) [22], Paglia and Valentile (1967) [23] and Golldberg., *et al.* (1983) [24] respectively.

Statistical analysis of data

Data were expressed as mean ± standard error (SE) for each experimental group. Statistical significance was analyzed by one-way ANOVA followed by Tukey's Multiple Comparisons. The p value of 0.05 was considered as the minimum level of significance.

Results

Ameliorative effects of CPLE on olanzapine-induced weight gain in rats

Treatment with olanzapine results in significant ($p < 0.05$) increase (27.5%) in body weight of the rats compare to the control rats (Table 1). Treatment of rats with CPLE reversed (23.4%) the olanzapine-induced weight gain with the most profound effect observed in the group administered 200 mg/kg bw CPLE and compared favourably with the group treated with orlistat.

Period (days)	Control	Obese + distilled water	Obese + Orlistat	Obese + 50 mg/kg BW CPLE	Obese + 100 mg/kg BW CPLE	Obese +200 mg/kg BW CPLE
0	142.60 ± 1.21^{a}	181.60 ± 0.93^{b}	181.60 ± 0.93^{b}	181.60 ± 2.81^{b}	181.20 ± 0.81^{b}	181.40 ± 1.21^{b}
7	156.80 ± 0.45^{a}	195.40 ± 4.29^{b}	175.2 ± 0.66^{c}	185.40 ± 0.24^{d}	178.40 ± 0.25^{e}	175.40 ± 1.24^{c}
14	166.20 ± 2.27^{a}	195.20 ± 3.43^{b}	168.4 ± 0.75^{c}	183.20 ± 0.50^{d}	175.20 ± 0.51^{e}	165.20 ± 0.93^{f}
21	174.50 ± 3.51^{a}	197.60 ± 4.68^{b}	165.2 ± 1.08^{c}	182.60 ± 0.75^{d}	167.60 ± 0.74^{c}	157.60 ± 0.73^{e}
28	180.40 ± 3.70^{a}	201.30 ± 4.16^{b}	154.6 ± 0.51^{c}	176.30 ± 0.49^{d}	165.80 ± 0.49^{e}	154.30 ± 0.68^{c}

Table 1: *Ameliorative effects of CPLE on olanzapine-induced weight gain in rats.*

Data were analysed by one-way ANOVA followed by Tukey's multiple comparison ($n = 5$, $p < 0.05$). Values are mean ± SE.

Ameliorative effects of CPLE on olanzapine-induced increase in BMI in rats

Olanzapine exposure results in significant increase (52.8%) in body mass index (BMI) of the rats compare to the control rats (Table 2). Treatment of rats with CPLE reversed (34.4%) the olanzapine-induced increase in BMI with the most profound effect observed in the group administered 200 mg/kg bw CPLE and compared favourably with the group treated with orlistat.

Period(day)	Control	Obese + distilled water	Obese+ Orlistat	Obese + 50 mg/kg BW CPLE	Obese + 100 mg/kg BW CPLE	Obese + 200 mg/kg BW CPLE
0	0.36 ± 0.02^{a}	0.55 ± 0.03^{b}	0.55 ± 0.02^{b}	0.55 ± 0.03^{b}	0.55 ± 0.02^{b}	0.55 ± 0.02^{b}
7	0.39 ± 0.04^{a}	0.57 ± 0.01^{b}	0.51 ± 0.02^{c}	0.57 ± 0.05^{b}	0.51 ± 0.04^{c}	0.49 ± 0.02^{c}
14	0.42 ± 0.06^{a}	0.58 ± 0.01^{b}	0.46 ± 0.04^{c}	0.56 ± 0.01^{b}	0.49 ± 0.03^{d}	0.44 ± 0.04^{c}
21	0.44 ± 0.09^{a}	0.60 ± 0.01^{b}	0.43 ± 0.01^{c}	0.54 ± 0.01^{d}	0.46 ± 0.04^{e}	0.42 ± 0.01^{c}
28	0.43 ± 0.01^{a}	0.61 ± 0.01^{b}	0.38 ± 0.03^{c}	0.54 ± 0.01^{d}	0.45 ± 0.03^{e}	0.40 ± 0.01^{c}

Table 2: *Ameliorative effects of CPLE on olanzapine-induced increase in BMI in rats.*

Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.

Effects of CPLE on olanzapine-induced increase in serum total cholesterol and triglycerides concentrations

Olanzapine exposure induced a marked increase in serum total cholesterol and triglycerides concentrations when compare to the control rats (Figure 1). Treatment of rats with CPLE reversed the olanzapine-induced increase in serum total cholesterol and triglycerides concentrations with the most profound effect observed in the group administered 200 mg/kg bw CPLE and compared favourably with the group treated with orlistat.

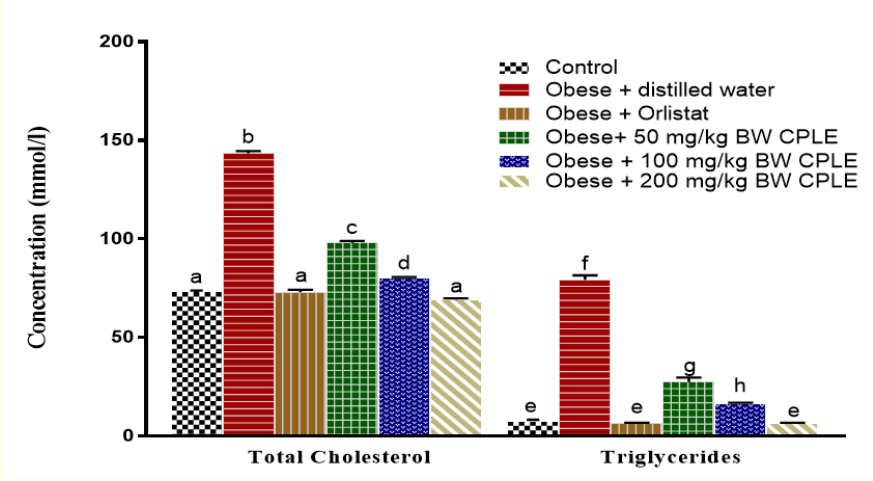

Figure 1: *Effects of CPLE on olanzapine-induced increase in serum total cholesterol and triglycerides concentrations. Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.*

Effects of CPLE on olanzapine-induced alterations in serum high and low density lipoprotein cholesterol concentrations

Exposure to olanzapine caused a distinct alteration in serum high density lipoprotein cholesterol and low density lipoprotein cholesterol concentrations when compare to the control rats (Figure 2). Treatment of rats with CPLE reversed the olanzapine-induced alterations in serum high density lipoprotein cholesterol and low density lipoprotein cholesterol concentrations with the best effect observed in the group administered 200 mg/kg bw CPLE even when compared with the group treated with orlistat.

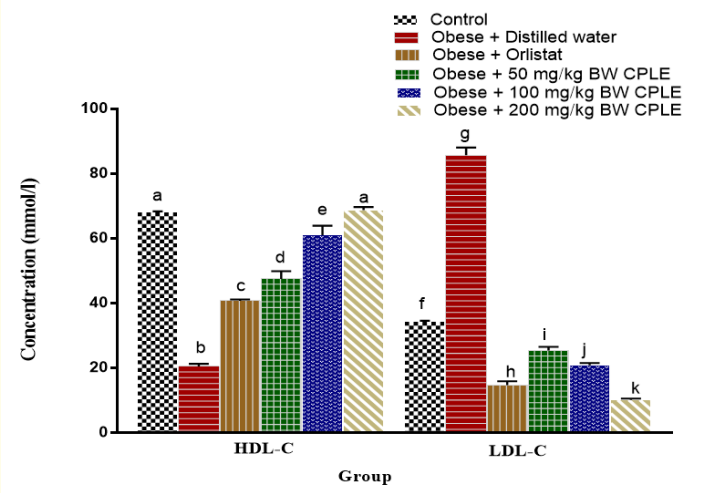

Figure 2: *Effects of CPLE on olanzapine-induced alterations in serum high and low density lipoprotein cholesterol concentrations. Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.*

Effects of CPLE on olanzapine-induced alterations in atherogenic indices

Exposure to olanzapine caused a divergent alteration in atherogenic indices when compare to the control rats (Table 3). Treatment of rats with CPLE reversed the olanzapine-induced alterations in atherogenic indices with the greatest effect observed in the group administered 200 mg/kg bw CPLE and compared favourably with the group treated with orlistat.

Group	AI	CRI	CRII
Control	0.02 ± 0.01^{a}	1.96 ± 0.01^{b}	0.10 ± 0.03^{a}
Obese + distilled water	0.39 ± 0.02^{b}	7.03 ± 0.24^{c}	4.20 ± 0.16^{b}
Obese + Orlistat	0.02 ± 0.01^{a}	1.79 ± 0.04^{b}	0.36 ± 0.03^{c}
Obese + 50 mg/kg bw CPLE	0.03 ± 0.01^{a}	2.08 ± 0.57^{c}	0.44 ± 0.13^{d}
Obese + 100 mg/kg bw CPLE	0.03 ± 0.01^{a}	1.32 ± 0.08^{b}	0.34 ± 0.12^{c}
Obese + 200 mg/kg bw CPLE	0.02 ± 0.01^{a}	0.90 ± 0.39^{a}	0.13 ± 0.06^{a}

Table 3: *Effects of CPLE on olanzapine-induced alterations in atherogenic indices.*

Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.

AI = Atherogenic index; CRI = Castelli risk index-I; CRII = Castelli risk index-II.

Effects of CPLE on olanzapine-induced increase in activity of creatine kinase

Treatment with olanzapine induced a marked elevation (48%) in creatine kinase activity when compare to the control rats (Figure 3). Treatment of rats with CPLE reversed the olanzapine-induced elevation in creatine kinase activity with best effects in groups administered 100 and 200 mg/kg bw CPLE respectively and even best when compared with the group treated with orlistat.

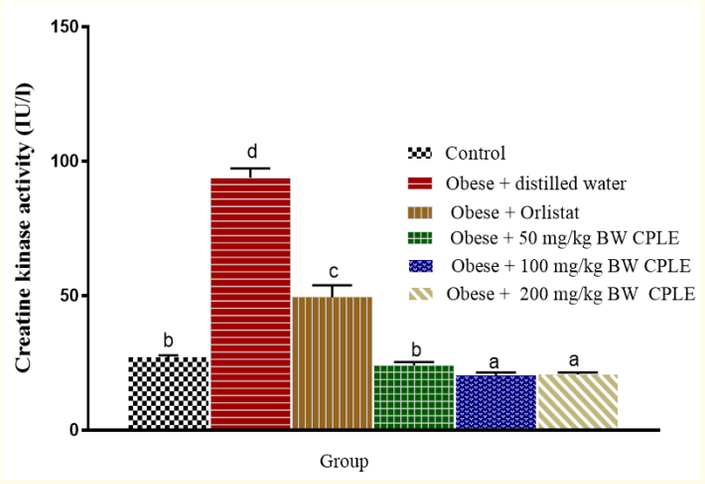

Figure 3: *Effects of CPLE on olanzapine-induced increase in activity of creatine kinase.*
Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.

Effects of CPLE on olanzapine-induced increase in lipase activity

Exposure of rats to olanzapine induced a significant elevation (48%) in lipase activity when compare to the control rats (Figure 4). Treatment of rats with CPLE reversed the olanzapine-induced elevation in lipase activity with the most profound effects in group administered 100 mg/kg bw CPLE respectively and compared favourably with group treated with orlistat.

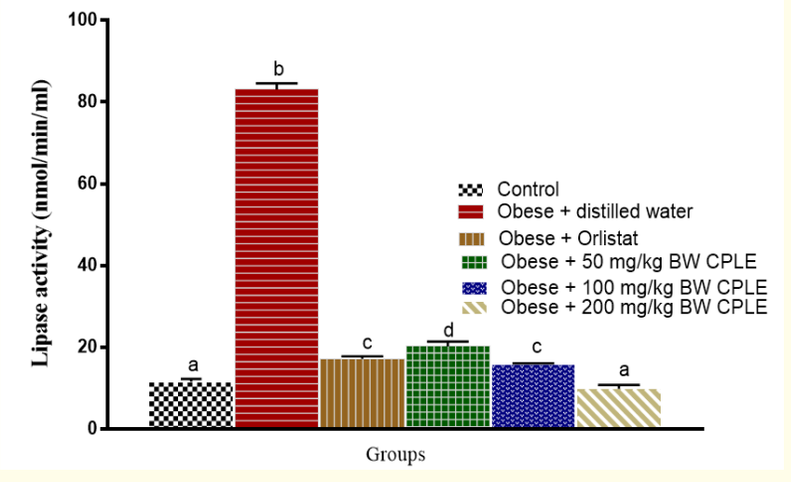

Figure 4: *Effects of CPLE on olanzapine-induced increase in lipase activity.*
Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.

Effects of CPLE on olanzapine-induced elevation in malondialdehyde concentration

Olanzapine exposure induced a marked increase in MDA levels in liver and heart of rats when compare to the control rats (Figure 5). Treatment of rats with CPLE reversed the olanzapine mediated increase in the levels of MDA. The decrease observed following treatment of rats with 50, 100 and 250 mg/kg bw was better than the group treated with orlistat.

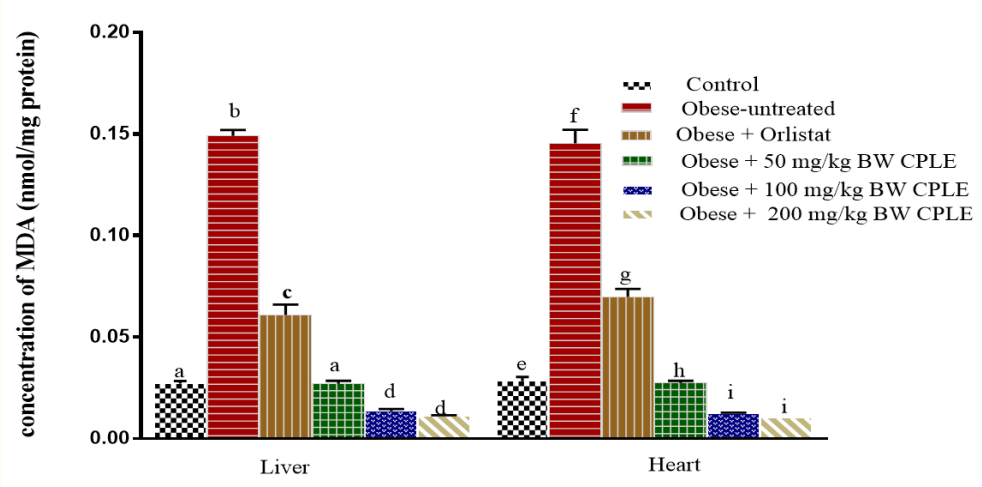

Figure 5: *Effects of CPLE on olanzapine-induced elevation in malondialdehyde (MDA) concentration. Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.*

Effects of CPLE on olanzapine-induced alterations in antioxidant enzymes activities

Olanzapine induced alteration in the activities of antioxidant enzymes was measured by assaying for the activity of CAT, SOD, GR and GPx which are enzymes involved in cell response to oxidative stress. Olanzapine treatment induced a significant depletion in the activities of CAT, SOD, GR and GPx in the liver and heart of rats (Table 4 and 5) when compared to the control. However, CPLE treatment boosted the antioxidant defense mechanism by increasing the activity of SOD, CAT, GR and GPx with the group treated with 200 mg/kg bw having the best effect even when compared with the group treated with orlistat.

Groups	Catalase (µmol/mg protein)	SOD (µmol/mg protein)	GR (µmol/mg protein)	GPx (µmol/mg protein)
Control	736.12 ± 6.27^{d}	247.64 ± 2.73^{d}	1.50 ± 0.23^{d}	24.42 ± 6.81^{d}
Obese + distilled water	34.10 ± 0.90^{a}	39.32 ± 1.96^{a}	0.20 ± 0.06^{a}	3.81 ± 2.43^{a}
Obese + Orlistat	219.10 ± 5.08^{b}	125.48 ± 1.70^{b}	0.57 ± 0.09^{b}	11.09 ± 5.27^{b}
Obese + 50 mg/kg bw CPLE	734.04 ± 6.31^{d}	245.40 ± 2.10^{d}	1.49 ± 0.06^{d}	25.18 ± 2.45^{d}
Obese + 100 mg/kg bw CPLE	550.90 ± 3.39^{c}	144.39 ± 2.26^{c}	0.67 ± 0.09 ^{c}	20.85 ±2.24^{c}
Obese + 200 mg/kg bw CPLE	740.17 ±0.36^{e}	315.85 ± 5.02^{e}	1.67 ± 0.03^{e}	30.32 ± 1.12^{e}

Table 4: *Effects of CPLE on olanzapine-induced alterations in liver antioxidant enzymes activities.*

Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.

Groups	Catalase (µmol/mg protein)	SOD (µmol/mg protein)	GR (µmol/mg protein)	GPx (µmol/mg protein)
Control	506.31 ± 1.12^{e}	251.42 ± b2.81^{e}	1.21 ± 0.06^{e}	20.57 ± 3.43^{d}
Obese + distilled water	180.99 ± 4.12^{a}	40.35 ± 1.77^{a}	0.47 ± 0.03^{a}	5.41 ± 1.17^{a}
Obese + Orlistat	220.42 ± 10.51^{b}	136.53 ± 1.96^{c}	0.65 ± 0.24^{b}	8.64 ± 4.07^{c}
Obese + 50 mg/kg bw CPLE	327.12 ± 3.39^{d}	141.25 ± 2.11^{d}	1.17 ± 0.09^{d}	8.22 ± 2.46^{c}
Obese + 100 mg/kg bw CPLE	319.67 ± 4.65^{c}	142.79 ± 3.79^{d}	0.74 ± 0.19^{c}	7.33 ± 1.02^{b}
Obese + 200 mg/kg bw CPLE	537.31 ± 8.71^{f}	318.25 ± 4.94^{f}	2.64 ± 0.12^{e}	28.94 ± 3.90^{e}

Table 5: *Effects of CPLE on olanzapine-induced alterations in heart antioxidant enzymes activities.*

Data were analysed by one-way ANOVA followed by Tukey's multiple comparison (n = 5, p < 0.05). Values are mean ± SE.

Discussion

Herbal medicines have received greater attention as alternative to clinical therapy and this has led to subsequent increase in their demands. In many communities, the use of herbal drugs in the treatment of various diseases is still very common. Cyathula prostrata has been used by herbal practitioners in the treatment of various diseases including obesity [25]. *Cyathula prostrata* leaf extract has been found to contain alkaloids, tannins, saponins, phenols, flavonoids and glycoside [26]. These metabolites have been linked with various roles in the management of obesity and other risk factors associated with obesity [27]. Olanzapine has been reported to cause significant weight gain in patients [28]. In this study, CPLE was able to reverse the increase in weight as a result olanzapine induction, the decreased in body weight with the administration of CPLE could be due to the presence of phenols, flavonoids and saponins as reported by Mopuri and Islam (2017) [27]. Administration of CPLE was found to reduce BMI that was induced by olanzapine administration, the reduction may be due to decrease in the activity of pancreatic lipase (Figure 4). The reduction in BMI can also be linked to the presence of phenols, saponins, flavonoids, tannins and alkaloids, studies have shown that these metabolites have various roles in the treatment of obesity [27,29,30]. Administration of CPLE brings about reduction in serum total cholesterol, triglycerides and LDL-c and increase in HDL-c the reduction associated with administration of CPLE implies that the extract has capability to ameliorate dyslipidaemia through cholesterol reducing effects, 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 [26]. This is supported by the work of Mopuri and Islam (2017) [27], who reported in their study that saponins have the ability to bind to cholesterol thereby causing depletion of body cholesterol, preventing its reabsorption and increasing its excretion from the body.

In this study lower levels of AI, CRI and CRII were observed in all the animals administered with CPLE, this implies that the extract has the ability to prevent the risk of cardiovascular diseases and this is strongly supported by the ability of the extract to reduce creatine kinase activity significantly better the reference drug.. It has been reported that lower levels of these indices are associated with lower risk of cardiovascular diseases [31,32]. Administration of CPLE significantly lower the creatine kinase activity when compare to the olanzapine-induced treated with distilled water, this is an indication that the extract has the ability to ameliorate the risk of pulmonary and myocardial infarction associated with obesity. It has been reported that elevated activities of creatine kinase (CK) are expressed in cardiac dysfunction pathophysiology such as in myocardial and pulmonary infarction, cerebrovascular-disease and electrical shocks [33].

The observed significant increase in lipase activity as a result of olanzapine induction is an indication of increase in the concentration of triglycerides which was observed in this study. Significant reduction in the activity of lipase following the administration of CPLE corresponds with decrease in the concentration of triglycerides observed with the administration of CPLE in this study. The finding is in line with the work of Hokason and Austin (2016) [34], who established in their study that decrease in lipase activity correspond with decrease

in triglycerides concentration. Olanzapine treatment resulted in significant increase in MDA concentration this may be attributed to oxidative stress imposed on the animal due to inability of the animal to scavenge the free radicals produced. The observed significant reduction in MDA concentration following the administration of CPLE could be attributed to the capability of the extract to detoxify free radicals produced as a result of oxidative stress [35].

Significant reduction in SOD, CAT, GR and GPx activities in the liver and heart as a result olanzapine treatment suggest an increasing production and continuous mopping up of free radicals. Obesity has been reported to be correlated to an increase in free radical generation as a result of oxidative stress or lipid peroxidation. The observed significant 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 and tannins [26] these metabolites have been reported to possess antioxidant effects [36,37].

Conclusion

It can be concluded from the findings of this study that the ability of CPLE to attenuate changes weight, lipid profiles, creatine kinase and lipase activities as well malondialdehyde and antioxidant enzymes activities strongly suggest its roles in ameliorating weight gain, lipid dysfunction, oxidative stress and alterations in antioxidant enzymes.

Bibliography

1. Blüher M. "Obesity: Global epidemiology and pathogenesis". *Nature Reviews Endocrinology* 15 (2019): 288-298.
2. World Health Organization (WHO). Obesity and overweight. Fact sheet (2018).
3. Bhavnani SM and Levin GM. "Antipsychotic agents: a survey of the prevalence, severity and burden of side effects". *International Journal of Clinical Psychopharmacology* 11 (1996): 1-12.
4. Dai H., *et al*. "The global burden of disease attributable to high body mass index in 195 countries and territories, 1990-2017: An analysis of the Global Burden of Disease Study". *PLoS Medicine* 17 (2020): 125-135.
5. Adewara SO., *et al*. "Decomposing inequality in the incidence of obesity in Nigeria". *International Journal of Development and Sustainability* 7.3 (2018): 1209-1219.
6. Kang JG and Park CY. "Anti-obesity drugs: A review about their effects and safety". *Journal of Diabetes and Metabolism* 36 (2012): 13-25.
7. Rodgers RJ., *et al*. "Antiobesity drugs: past, present and future". *Disease Model Mechanism* 5.5 (2012): 621-626.
8. Iwu MM. "Handbook of African Medicinal Plants". Boca Raton: CRC Press (1993): 1-9.
9. Smith AC. "Flora Vitiensis nova: a new flora of Fiji". National Tropical Botanical Garden, Lawai, Kauai, Hawaii 2 (1981): 810.
10. Anthony BO., *et al*. "Cyathula prostrata: a potential herbal hope for hypertensive, an Animal model study and its secondary metabolites assessment via ac-ms". *European Journal of Medical Plants* 14.2 (2016): 1-10.
11. Novelli ELB., *et al*. "Anthropometrical parameters and markers of obesity in rats". *Laboratory Animals* 41.1 (2007): 111-119.
12. Fredrickson DS., *et al*. "Fat transport in lipoproteins- An integrated approach to mechanisms and disorders". *New England Journal of Medicine* 276 (1967): 148-156.

13. Tietz NW. "Clinical Guide to Laboratory Tests, 2nd edition., W. B". Saunders Company, Philadelphia, USA (1990): 554-556.

14. Tietz NW. "Fundamental of Clinical Chemistry, W. B". Saunders Company, Philadelphia, USA (1976): 723.

15. Albers JJ., *et al*. "Quantization of high density Lipoproteins". *Lipids* 13 (1978): 926-932.

16. Kuldip S and Ahluwalia P. "Effect of monosodium glutamate on lipid peroxidation and certain antioxidant enzymes in cardiac tissue of alcoholic adult male mice". *Journal of Cardiovascular Disease Research* 3.1 (2012): 215-221.

17. Castelli WP., *et al*. "Summary estimates of cholesterol used to predict coronary heart disease". *Circulation* 67.4 (1983): 730-734.

18. Tietz NW. "Textbook of Clinical Chemistry, W.B". Saunders, Philadelphia, PA (1986): 305-310.

19. Gu Y., *et al*. "Inhibition of key digestive enzymes by Cocoa extracts and Procyanidins". *Journal of Agricultural Food Chemistry* 59 (2011): 5305-5311.

20. Ohkawa H., *et al*. "Assay for lipid peroxidation in animal tissues by thiobarbituric acid reaction". *Analytical Biochemistry* 95 (1979): 351-359.

21. Misra HP and Fridovich I. "The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase". *Journal of Biological Chemistry* 247 (1972): 3170-3175.

22. Beers RF and Siser IW. "A spectrophotometric method for measuring breakdown of hydrogen peroxide by catalase". *Journal of Biological Chemistry* 195 (1952): 133-140.

23. Paglia DE and Valentine WN. "Studies on the quantitative and qualitative characterisation of erythrocyte glutathione peroxidase". *Journal of Laboratory and Clinical Medicine* 70 (1967): 158-69.

24. Goldberg DM., *et al*. In Methods of Enzymatic Analysis 3rd edition (1983): 258-226.

25. Ogbonnia SO., *et al*. "Evaluation of Acute Toxicity and Hypoglycaemic and Hypolipidaemic Effects of Cyathula prostata (Linn.) Blume Weeds on Adult Rats". *British Journal of Pharmaceutical Research* 9.5 (2016): 1-11.

26. Hassan RI., *et al*. "Protective effects of Cyathula prostrata leaf extract on olanzapine-induced obese rats". *The Journal of Phytopharmacology* 10.2 (2021): 68-79.

27. Mopuri R and Islam MS. "Medicinal plants and phytochemicals with obesogenic potential: A review". *Biomedicine and Pharmacotherapy* 89.2 (2017): 1442-1452.

28. Vander Zwaal EM., *et al*. "Modelling olanzapine-induced weight gain in rats". *International Journal of Neuropsychopharmacology* 17 (2014): 169-186.

29. Sharma T and Kanwar SS. "Phytomolecules for Obesity and Body Weight Management". *Journal Biochemistry and Cell Biology* 1 (2018): 101.

30. Feng L., *et al*. "Hypolipidemic and antioxidant effects of total flavonoids of Perilla frutescens leaves in hyperlipidemia rats induced by high fat diet". *Food Resources International* 44 (2011): 404-409.

31. Dobiasova M., *et al*. "Cholesterol esterification and atherogenic index of plasma correlate with lipoprotein size and findings on coronary angiography". *Journal of Lipid Research* 52 (2011): 566-571.

32. Khazaál MS. "Atherogenic Index of Plasma (AIP) as a parameter in predicting cardiovascular risk in males compared to the conventional dyslipidemic indices (cholesterol ratios)". *Karbala Journal of Medicine* 6.1 (2013): 1506-1513.

33. Bagale KR., *et al*. "Contributions of various lipid profile parameter in determining creatine kinase levels in unstable angina patients". *International Journal of Applied and Basic Medical Research* 6.2 (2016): 106-110.

34. Hokanson JE and Austin MA. "Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies". *Journal of Cardiovascular Risk* 3 (2016): 213- 219.

35. Ferri M., *et al*. "Recovery of polyphenols from red grape pomace and assessment of their antioxidant and anti-Cholesterol activities". *Nutritional Biotechnology* 33 (2016): 338-44.

36. Sonibare MA and Olatubosun OV. "Pharmacognostic and free radical scavenging Evaluation of Cyathula prostata (Blume) L". *Pharmacognostic Journal* 7.2 (2017): 107-116.

37. Ibrahim B., *et al*. "Anti-inflammatory, analgesic and antioxidant activities of Cyathula prostrate (Linn) Blume (Amaranthaceae)". *Journal of Ethnopharmacology* 141.1 (2015): 282-289.

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