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Biochemical Profile of Albino Rats with Experimentally-Induced Metabolic Syndrome Fed Diet Formulations of *Cnidoscolus aconitifolius*, *Gongronema latifolium* and *Moringa oleifera* Leaves †

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Abstract: This study evaluated the effect of diet formulations of *Gongronema latifolium* leaf (GLL), *Cnidoscolus aconitifolius* leaf (CAL) and *Moringa oleifera* leaf (MOL) on biochemical parameters of experimentally-induced MS in male albino rats. Adult Wistar rats (forty-eight) 180–210 g were randomly grouped into eight groups of six rats each. Group 1 received normal diet. MS was induced in experimental rats (Groups 2–8) using high fat high carbohydrate (HFHC) diet for eight weeks, then group 2 was fed normal rat diet (untreated), while groups 3 to 8 was treated with diets formulated with GLL, CAL, MOL for another eight weeks. The dose of the plants used for feed formulation was 10% of the formulated diet for each treatment. Antioxidant status, liver enzymes, lipid profile and obesity indices were evaluated using standard methods. Superoxide dismutase and catalase activities significantly ($p < 0.05$) increased in the treatment groups. Significant ($p < 0.05$) decrease in total cholesterol, triacylglycerols and body weight gain of the treated groups were observed, high density lipoprotein significantly ($p < 0.05$) increased compared to the untreated group. Results from the study indicate that GLL, CAL, and MOL have therapeutic potentials that could be useful in the management of metabolic syndrome.

Keywords: high fat high carbohydrate diet; antioxidant status; metabolic syndrome; lipid profile; *Cnidoscolus aconitifolius*

1. Introduction

Metabolic syndrome (MS), has become a major public health concern worldwide, due to increasing urbanization with its attendant influence on individuals towards surplus energy intake and sedentary lifestyle. It involves multiple metabolic pathways, having insulin resistance and central obesity as its underlying risk factors with other disorders such as: dyslipidaemia,

hypertension and microalbuminuria [1–3]. MS has been defined as a cluster of metabolic and clinical abnormalities that directly increase the risk of type 2 diabetes and atherosclerotic cardiovascular disease with attendant mortality [1,4]. The abnormalities include: obesity, dyslipidemia, glucose intolerance, microalbuminuria, hypertension and glucose intolerance. Patients with MS are five times more likely to develop type 2 diabetes, and twice more at risk for cardiovascular mortality than those without the disorder [5,6].

The global prevalence of MS ranges from <10% to about >80%, varying based on the region, location (urban or rural area), composition of the population (gender, age, ethnicity, race), and the delineating parameters of the syndrome used in the study [7]. Available data show that MS affects 25% of the entire world population of adults. Differences in diet consumption, genetic factors, environment, and levels of physical activity contribute to the prevalence of MS and its various components [8]. The clinical management of MS is usually difficult because there is no known method used to prevent or manage the whole syndrome. Hence, successful treatment/management of MS is usually targeted at the individual MS components using lipid and glucose lowering agents, antihypertensive agents as well as insulin sensitizers [7,9].

Increased use of herbal medicine has been documented with about 80% of rural dwellers in developing countries solely depending on it for basic health care [10]. In addition to the presence of biological activity which is exploited in managing several diseases, use of herbs present little or no adverse effects [11]. *Gongronema latifolium* leaves (GLL) and *Moringa oleifera* leaves (MOL) possess various nutritional and medicinal values and have been used widely in treatment of disorders associated with MS. The presence of some bioactive components has been reported in these plants which formed the basis for the choice. This study investigated the effect of diet formulations of GLL, CAL and MOL on some biochemical parameters in experimentally-induced metabolic syndrome in male albino rats.

2. Experiments

Animals

Forty-eight (48) adult male Wistar rats weighing between 180–210 g were obtained from the animal house of the Faculty of Biological Sciences, University of Nigeria, Nsukka (UNN). The rats were housed at room temperature on a 12-h dark-light cycle and acclimatized for 14-days with *ad libitum* access to food (rat diet) and water. Ethical approval for the study regarding the use of experimental animals was obtained from the Ethics and Biosafety Committee of the Faculty of Biological Sciences, University of Nigeria, Nsukka with reference number UNN/FBS/EC/1028.

Collection, Identification and Processing of Plant Materials

Leaf samples of *Gongronema latifolium* and *Moringa oleifera* were obtained from Ogige Market and Obukpa respectively, both in Nsukka; while *Cnidoscolus aconitifolius* was collected from a vegetable garden in University of Nigeria, Nsukka. The plant materials were air-dried, pulverized and packaged in air-tight-polyethene bags and stored at room temperature prior to use.

Induction of Metabolic Syndrome

The rats were fed with high-fat high-carbohydrate (HFHC) diet which is made up of high fat diet and 20% fructose drinking water (FDW) for eight (8) weeks to induce metabolic syndrome. The high fat diet formulation method was adapted from [6] as follows: carbohydrate—200 g/kg, protein—250 g/kg, fat—500 g/kg, fibre—40 g/kg, vitamin-mineral mix—10 g/kg. FDW was freshly prepared every other day by dissolving 20 g of fructose in 100 mL of tap water [12,13] and administered ad libitum

Formulation and Administration of Rat Diets

Cnidoscolus aconitifolius leaves (CAL), *Gongronema latifolium* leaves (GLL) and *Moringa oleifera* leaves (MOL) were used in the formulation of rat diets for treatment. After the establishment of MS,

rats were divided into eight groups of six rats each and fed group specific diets for eight (8) weeks as follows:

Group 1: Commercial rat diet and tap water—Normal control
Group 2: MS rats fed commercial rat diet and tap water—Untreated control
Group 3: MS rats fed diet with CAL and tap water
Group 4: MS rats fed diet with GLL and tap water
Group 5: MS rats fed diet with MOL and tap water
Group 6: MS rats fed with combined CAL and GLL (1:1) diet and tap water
Group 7: MS rats fed with combined GLL and MOL (1:1) diet and tap water
Group 8: MS rats fed with combined CAL and MOL (1:1) diet and tap water

The dose of the plants used for feed formulation was 10%, which is 100 g of plant in 1000 g of the total formulated diet for each treatment.

Samples Collection

At the end of treatment duration, the animals were sacrificed after being anaesthetized using chloroform. Blood samples were drawn via cardiac puncture into non-heparinized sample tubes, allowed to stand for about 15 min to clot and centrifuged at 4000 rpm for 10 min. The supernatant (serum) was collected and stored at −20 °C for the biochemical tests. The liver of the rats was carefully excised, weighed and prepared for histopathological study.

Oxidative Stress Index and Antioxidant Enzymes Activities

Malondialdehyde (MDA), Superoxide dismutase (SOD) and catalase (CAT) activities were determined using standard methods.

Liver Function Tests

Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), total protein and albumin were determined using the standard methods as outlined in the assay kits leaflets.

Determination of Serum Lipid Profile

The serum lipid parameters including total cholesterol (TC), triacylglycerol (TAG) and high-density lipoprotein cholesterol (HDL-C) were determined using standard methods.

Measurement of Obesity Indices

Body weight and height were measured and body mass index (BMI) was calculated using standard methods. The rats were anaesthetized using diethyl ether inhalation prior to taking the measurements [14].

Statistical Analysis

All data were analyzed using the IBM SPSS Statistics software (version 23) and presented as means ± standard deviation (SD). One-way analysis of variance (ANOVA) was used to analyze the data obtained and Duncan multiple range test was used to separate homogenous means. Differences were considered significant at $p < 0.05$.

3. Results

3.1. Effect of C. aconitifolius, G. latifolium and M. oleifera-Based Diets on Serum Malondialdehyde (MDA) and Antioxidant Enzymes of Rats with Experimentally-Induced Metabolic Syndrome

There was no significant ($p > 0.05$) difference in MDA concentration of all the test groups when compared to the untreated control. Treatment with MOL, CAL + GLL, GLL + MOL and CAL + MOL significantly ($p < 0.05$) increased SOD activity compared with the untreated group. There was a

significant ($p < 0.05$) increase in catalase activity in all the treated groups compared with untreated control, except for the MOL- and CAL + GLL-treated groups (Table 1).

Table 1. Effect of *C. aconitifolius*, *G. latifolium* and *M. oleifera*-based diets on MDA and antioxidant enzymes of rats with experimentally-induced metabolic syndrome.

Group	MDA (U/mg Protein)	SOD (IU/mg Protein)	CAT (IU/mg Protein)
1. Normal	6.43 ± 0.76 [a]	74.51 ± 3.17 [a,b]	0.66 ± 0.10 [a]
2. Untreated	7.15 ± 3.16 [a]	42.85 ± 10.52 [a]	1.38 ± 0.73 [a,b]
3. CAL	6.63 ± 2.47 [a]	56.97 ± 12.75 [a]	2.54 ± 0.06 [c]
4. GLL	5.19 ± 0.81 [a]	54.35 ± 15.58 [a]	1.98 ± 0.56 [b,c]
5. MOL	6.96 ± 4.68 [a]	101.24 ± 13.99 [b]	1.10 ± 0.32 [a,b]
6. CAL + GLL	7.80 ± 0.16 [a]	131.88 ± 36.46 [b]	1.78 ± 0.54 [b]
7. GLL + MOL	10.89 ± 2.73 [a]	76.97 ± 11.29 [a,b]	2.47 ± 0.68 [c]
8. CAL + MOL	11.88 ± 5.05 [a]	131.16 ± 37.19 [b]	2.28 ± 0.64 [b,c]

Each value represents mean ± SD. n = 3. Mean values with different alphabets as superscripts in a column are statistically significant ($p < 0.05$).

3.2. Effect of C. aconitifolius, G. latifolium and M. oleifera-Based Diets on Liver Function Markers of Rats with Experimentally-Induced Metabolic Syndrome

AST activity was significantly ($p < 0.05$) higher in rats treated with single herb diets (CAL, GLL, MOL), while that of rats treated with herbs in combination (CAL + GLL, GLL + MOL, CAL + MOL) was not significantly different compared with untreated control (Table 2). No significant ($p > 0.05$) changes was observed in ALT activity of all the treatment groups compared with the untreated control. ALP activity showed a significant ($p < 0.05$) increase in the treatment groups compared with the untreated group. Total protein concentrations of the treated rats were not significantly ($p > 0.05$) changed compared to the untreated group. Albumin concentration significantly ($p < 0.05$) decreased in rats administered CAL, CAL + GLL, GLL + MOL and CAL + MOL compared with the control groups (Table 2).

Table 2. Effect of *C. aconitifolius*, *G. latifolium* and *M. oleifera*-based diets on liver function markers of rats with experimentally-induced metabolic syndrome.

Group	AST (U/L)	ALT (U/L)	ALP (U/L)	Total Protein (g/dL)	Albumin (g/dL)
1. Normal	19.89 ± 1.99 [a]	11.53 ±3.15 [a]	7.95 ± 0.98 [b,c]	3.02 ± 0.70 [a,b]	2.57 ± 0.33 [b]
2. Untreated	20.21± 2.00 [a]	8.48 ±0.16 [a]	3.78 ± 0.16 [a]	3.68 ± 0.81 [a,b]	3.02 ± 0.08 [b]
3. CAL	34.53 ± 3.80 [b,c]	20.50 ± 3.08 [a]	5.96 ± 0.59 [a,b]	3.48 ± 0.08 [a,b]	2.49 ± 0.43 [a]
4. GLL	33.73 ± 3.72 [b,c]	10.24 ± 0.64 [a]	6.06 ± 0.43 [a,b]	3.27 ± 0.50 [a,b]	3.07 ± 0.76 [b,c]
5. MOL	37.44 ± 0.36 [c]	14.75 ± 4.22 [a]	8.90 ± 1.98 [c]	4.27 ± 0.75 [a,b]	3.07 ± 0.02 [b,c]
6. CAL + GLL	20.75 ± 2.81 [a]	15.19 ± 4.07 [a]	9.09 ± 0.28 [c]	4.18 ± 0.65 [a,b]	2.33 ± 0.44 [a]
7. GLL + MOL	22.21 ± 3.18 [a]	13.18 ± 4.27 [a]	9.46 ± 0.99 [c]	2.92 ± 0.43 [a,b]	1.90 ± 0.53 [a]
8. CAL + MOL	25.98 ± 0.67 [a,b]	20.16 ± 3.47 [a]	8.61 ± 0.84 [c]	4.85 ± 2.09 [b]	1.35 ± 0.16 [a]

Each value represents mean ± SD. n = 3. Mean values with different alphabets as superscripts in a column are statistically significant ($p < 0.05$).

3.3. Effect of C. aconitifolius, G. latifolium and M. oleifera-Based Diets on Serum Lipid Profile of Rats with Experimentally-Induced Metabolic Syndrome

The rats treated GLL, MOL, CAL + GLL, GLL + MOL, and CAL + MOL had a significant ($p < 0.05$) decrease in mean TC compared with the untreated control (Table 3). TAG concentrations of all the treated groups except for the CAL-treated were significantly ($p < 0.05$) lower than that of the untreated control. There was a significant ($p < 0.05$) increase in the mean HDL-C concentrations of rats administered CAL, GLL + MOL and CAL + MOL compared with untreated control and an

increase. The LDL-C concentrations of the CAL and GLL + MOL groups significantly ($p < 0.05$) decreased compared to the untreated group.

Table 3. Effect of *C. aconitifolius*, *G. latifolium* and *M. oleifera*-based diets on lipid profile of rats with experimentally-induced metabolic syndrome.

Group	TC (mg/dL)	TAG (mg/dL)	HDL-C (mg/dL)
1. Normal	133.33 ± 13.33 ^{b,c}	120.27 ± 9.74 ^{d}	90.40 ± 13.80 ^{b}
2. Untreated	144.00 ± 20.13 ^{c,d}	101.73 ± 10.13 ^{c}	90.40 ± 5.2 ^{b}
3. CAL	162.66 ± 14.84 ^{d,e}	102.84 ± 1.01 ^{c}	141.62 ± 21.09 ^{c}
4. GLL	114.66 ± 7.05 ^{a,b}	89.82 ± 10.13 ^{a,b}	102.45 ± 13.13 ^{b}
5. MOL	96.00 ± 4.61 ^{a}	94.45 ± 10.70 ^{a,b}	51.22 ± 3.01 ^{a}
6. CAL + GLL	82.66 ± 5.33 ^{a}	70.62 ± 0.76 ^{a}	102.45 ± 6.02 ^{b}
7. GLL + MOL	136.00 ± 16.65 ^{b,c}	76.57 ± 4.50 ^{a}	117.52 ±13.80 ^{c}
8. CAL + MOL	122.66 ± 11.62 ^{a,b}	95.77 ± 10.73 ^{a,b}	180.80 ± 9.04 ^{c}

Each value represents mean ± SD. n = 3. Mean values with different alphabets as superscripts in a column are statistically significant ($p < 0.05$).

3.4. Effect of C. aconitifolius, G. latifolium and M. oleifera-Based Diets on Obesity Indices of Rats with Experimentally-Induced Metabolic Syndrome

The different diet formulations significantly ($p < 0.05$) decreased the body weights of the rats in the treatment groups compared to the untreated control (Table 4). The BMI of the diet-fed rats were significantly ($p < 0.05$) lower than that of the normal control but not significantly ($p > 0.05$) different from the untreated control (Table 5).

Table 4. Effect of *C. aconitifolius*, *G. latifolium* and *M. oleifera*-based diets on body weight of rats with experimentally-induced metabolic syndrome.

Group	Initial Body Weight (g)	Final Body Wt (g)	Body Wt Gain (g)
1. Normal Ctrl	244.66 ± 10.50 ^{a}	301.66 ± 12.58 ^{a}	57.00 ± 2.64 ^{a}
2. Untreated Ctrl	282.66 ± 7.02 ^{b}	381.66 ± 2.88 ^{c}	99.00 ± 9.53 ^{b}
3. CAL	290.00 ± 4.00 ^{c}	350.33 ± 2.51 ^{b}	60.33 ± 3.78 ^{a}
4. GLL	276.66 ± 6.65 ^{b}	334.33 ± 12.09 ^{b}	57.66 ± 8.62 ^{a}
5. MOL	274.00 ± 12.16 ^{b}	334.33 ± 12.09 ^{b}	60.33 ± 2.51 ^{a}
6. CAL + GLL	293.33 ± 3.21 ^{c}	356.66 ± 10.40 ^{b}	63.33 ± 8.08 ^{a}
7. GLL + MOL	283.66 ± 7.23 ^{b}	346.67 ± 5.68 ^{b}	63.00 ± 2.00 ^{a}
8. CAL + MOL	282.00 ± 6.08 ^{b}	341.67 ± 33.29 ^{b}	59.66 ± 22.36 ^{a}

Each value represents mean ± SD. n = 3. Mean values with different alphabets as superscripts in a column are statistically significant ($p < 0.05$).

Table 5. Effect of *C. aconitifolius*, *G. latifolium* and *M. oleifera*-based diets on body mass index (BMI) of rats with experimentally-induced metabolic syndrome.

Group	Initial BMI (g/cm^2)	Final BMI (g/cm^2)	BMI Gain (g)
1. Normal Ctrl	0.49 ± 0.03 ^{a}	0.62 ± 0.08 ^{b}	0.13 ± 0.06 ^{b}
2. Untreated Ctrl	0.53 ± 0.01 ^{b}	0.59 ± 0.02 ^{a}	0.06 ± 0.04 ^{a}
3. CAL	0.52 ± 0.02 ^{b}	0.56 ± 0.01 ^{a}	0.04 ± 0.02 ^{a}
4. GLL	0.50 ± 0.00 ^{b}	0.53 ± 0.02 ^{a}	0.03 ± 0.01 ^{a}
5. MOL	0.51 ± 0.02 ^{b}	0.53 ± 0.01 ^{a}	0.02 ± 0.01 ^{a}
6. CAL + GLL	0.51 ± 0.01 ^{b}	0.58 ± 0.04 ^{a}	0.07 ± 0.03 ^{a}
7. GLL + MOL	0.49 ± 0.01 ^{a}	0.54 ± 0.01 ^{a}	0.04 ± 0.02 ^{a}
8. CAL + MOL	0.51 ± 0.01 ^{b}	0.56 ± 0.01 ^{a}	0.05 ± 0.01 ^{a}

Each value represents mean ± SD. n = 3. Mean values with different alphabets as superscripts in a column are statistically significant ($p < 0.05$).

4. Discussion

Metabolic syndrome (MS) manifests with obesity as one of its important risk factors. Thus, interventions that target body weight reduction are useful in management of MS. The findings of this study suggest that the diet formulations of *C. aconitifolius*, *G. latifolium* and *M. oleifera* had a weight reducing effect on the rats. Weight-reducing ability of plants has been attributed to the presence of polyphenols, which contributes to the prevention and treatment of many disease conditions including obesity [15]. Thus, the high polyphenol (flavonoid) content of *C. aconitifolius*, *G. latifolium* and *M. oleifera* could be responsible for the observed body weight-limiting effect. This finding agrees with that of [16] who reported a significant ($p < 0.05$) decrease in body weight gain after the treatment of obese rats with aqueous extracts of green tea (*Camellia sinensis*), which is known to contain appreciable quantity of polyphenols.

Over time, research has revealed that free radicals are predisposing factors to some human diseases such as obesity, diabetes, atherosclerosis and other cardiovascular diseases. Oxidative stress is strongly associated with damage in the body caused by free radicals. These free radicals adversely affect cell integrity as a result of membrane damage through the oxidative damage of lipids, protein and irreversible DNA modification [17]. Treatment of MS rats with diets formulated with the leaves of *M. oleifera*, *G. latifolium* and *C. aconitifolius* singly, caused a reduction though not significant ($p > 0.05$) in serum levels of MDA. When combined, the serum MDA levels were also not significantly ($p > 0.05$) changed compared to the untreated control. Consumption of these plants (in combination) was not able to alter MDA level significantly despite their flavonoid content. The arrangement and composition of the chemical structure of flavonoids play key roles in their antioxidant and free radical scavenging activities. One would have expected a synergistic effect resulting in marked reduction of MDA levels when the herbs were used as a combined therapy, however, the reverse was the case. The interaction of the varied bioactive components with each other and the anti-nutrients present in the plants may have either reduced the availability or inhibited the absorption of the particular antioxidant compounds needed.

In addition to lipid peroxidation, oxidative stress is characterized by the decrease in activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione S-transferase (GST), and glutathione peroxidase (GPx) which help to mop up free radicals in conditions of oxidative stress [18]. Reduction in activity of antioxidant enzymes may be as a result of quick mobilization and complete utilization of the reserve of these enzymes in mopping up free radicals generated during the development of MS. Similar studies have reported significant antioxidant property of some other plants on serum, kidney and liver SOD and catalase activities in rats fed a high fat diet [19]. The antioxidant properties of plants are attributed mainly to their phenolic compounds.

This diet-induced increase in liver enzyme activities was relatively reduced with the consumption of diet formulations using the herbs *Moringa*, *Gongronema* and *Cnidoscolus*. This proves the efficacy of these herbs when used in combination as polyherbal therapy. The groups treated with single dose of *G. latifolium* and the combinations of *G. latifolium* with the other herbs were more effective in decreasing the serum ALT activity. The synergistic antioxidant property of flavonoidal compounds in *M. oleifera, G. latifolium* and *C. aconitifolius* contributed to the decrease in the oxidative stress in liver and also increased the levels of the antioxidant enzymes, catalase and SOD [19].

Treatment of rats with the leaves of *M. oleifera, G. latifolium* and *C. aconitifolius* significantly ($p < 0.05$) decreased the concentration of serum lipids (total cholesterol and TAG) indicating the potential of these herbs to help decrease the incidence of cardiovascular diseases. This is in line with previous reports on the use of *M. oleifera* and *G. latifolium* leaf extracts in the management of hyperlipidaemia [20] indicating that the herbs could decrease the formation of triacylglycerols in the liver whilst helping in the redistribution of cholesterol. Low concentration of HDL-cholesterol predisposes to cardiovascular disease. HDL has cardio-protective properties because it plays an important role in mopping up excess cholesterol from peripheral tissues by reverse cholesterol transport [21]. The observed increase in HDL-C in the treatment groups is in line with the findings of [22] who studied

the effect of diet incorporated with leaves of *G. latifolium* and *V. amygdalina* on the lipid profiles of rats. They reported a significant ($p < 0.05$) decrease in serum TC and TAG and a significant ($p < 0.05$) increase in HDL-C.

5. Conclusions

The utilization of feed formulations of *Cnidoscolus aconifolius, Gongronema latifolium* and *Moringa oleifera* in the treatment of rats with experimentally induced metabolic syndrome in this study showed reduction in the metabolic and cardiovascular risks in terms of weight reduction, favourable lipid profile as well as increase in the activities of antioxidant enzymes (superoxide dismutase and catalase). Thus, the herbs have some therapeutic effects and could be useful in the management of metabolic syndrome components.

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