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The effect of extracts of *Irvingia gabonensis* (IGOB131) and *Dichrostachys glomerata* (Dyglomera™) on body weight and lipid parameters of healthy overweight participants

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ABSTRACT

Background: Previous work reported the benefits of extracts of 2 Cameroonian spices – *Irvingia gabonensis* and *Dichrostachys glomerata*— on obese people with metabolic syndrome. Considering the physio-metabolic changes that accompany obesity, the present study investigates the effects of these extracts on healthy overweight participants over an 8-week test period.

Methods: The study was an 8 week randomized double-blind, placebo controlled design involving 48 overweight (BMI 26 – 30) participants (27 females and 19 males), divided into 3 groups – placebo, 300 mg *I. gabonensis* extract (IGOB131), or 300 mg *D. glomerata* extract (Dyglomera™). Capsules containing the placebo or the test formulations were administered once daily before the main meal of the day. No major dietary changes or changes in physical activity were demonstrated during the study. Weight and blood lipid parameters were measured at baseline, and at the 4 and 8 weeks interval.

Results: Compared to the placebo group, there were significant ($p<0.05$) reductions in weight of participants in both test groups over the 8 week period. However, these significant changes were not observed in the initial 4 weeks, even though the lipid parameters in the test groups changed significantly ($p<0.05$).

Conclusion: The extracts of *Irvingia gabonensis* and *Dichrostachys glomerata*, at a dose of 300 mg per day, were effective in reducing weight and positively modifying lipid parameters in healthy overweight participants.

Keywords: Overweight, *Dichrostachys*, *Irvingia*, waist-hip circumference, blood lipids.

INTRODUCTION

Obesity is a multifaceted disease which generally leads to several complications and increased morbidity and mortality related to coronary heart diseases, diabetes type 2, metabolic syndrome, stroke and cancers [1, 2]. To become obese, healthy individuals generally experience progression from normal weight, to being overweight (considered generally as being healthy), and finally to obese (considered as being an unhealthy or diseased state). Treatment or management of obesity is difficult, due the complexity of associated complications. Therefore, attempts to prevent progression in body weight and fat accumulation, from an overweight/pre-obese condition to obesity, can lower worldwide mortality rates related to obesity. This study investigates the effects of the extracts of *Irvingia gabonensis* (IGOB131) and *Dichrostachys glomerata* (Dyglomera^{TM}) on healthy overweight participants over an 8-week test period.

PARTICIPANTS AND METHODS

A total of 48 overweight participants aged between 23 and 55 years were selected from a group of 220 overweight and obese persons responding to a radio advertisement in Yaoundé, Cameroon. After physical examination and laboratory screening tests, diabetics, pregnant and lactating women were excluded. All participants were judged as healthy (normal range of temperature, no clinical consultation within the previous 2 weeks) by the resident physician, and were not on any weight reducing protocol. The purpose, nature and potential risks of the study were explained to all patients and a written informed consent was obtained before their participation. The local research ethics committee approved the experimental protocol.

Study design: Participants were given one of three different types of capsules containing either 300mg of *Irvingia gabonensis* extract (***IGOB131,*** *with ≥7% albumin and ≥1% ellagic acid*), 300 mg of hydroethanolic (90:10, water :ethanol) extract of *Dichrostachys glomerata* (***Dyglomera™***) or oat bran (**placebo**). The capsules were taken one-half hour before the main meal with a glass of warm water. Capsules were identical in shape, colour, and appearance, with neither participant nor researchers knowing what capsule they received. During the 8 week experimental period, participants were examined weekly, with their body weight, body fat, waist and hip circumferences recorded each time. Subjective findings, such as increased or decreased appetite, feeling of lightness and gastrointestinal pains, were individually noted. The participants were also interviewed about their physical activity and food intake during the trial, and were instructed not to modify these habits.

Anthropometric measurements: The heights of participants were measured during the first visit and their weights at each subsequent visit. BMI was also calculated, and served as a basis of inclusion or exclusion in the study. The percent body fat was measured with a Tanita™ BC-418

Body Composition Analyzer/Scale, while waist and hip circumferences were measured with a soft non-stretchable plastic tape. In an effort to ensure intra-individual consistency, the participants were measured at approximately the same time of the day for each visit.

Laboratory methods: Blood samples were collected after a 12h overnight fast into heparinized tubes at the beginning of the study, after four weeks, and at the end (8 weeks) of treatment. The concentrations of total cholesterol, triacylglycerol, HDL-cholesterol, in plasma were measured using a commercial diagnostic kit (Cholesterol infinity, triglycerides Int, EZ HDL^{TM} cholesterol from SIGMA Diagnostics. LDL–cholesterol values were calculated using the Friedwald equation.

Statistical Analysis: Results are expressed as mean ± SEM. Paired Student's t-test was used on the start and end values of placebo and test capsules, and also on the differences between the placebo and test groups. In the tables in the same row, values with different letters (a, b) are significantly different at $p < 0.05$ and $p < 0.01$ respectively.

RESULTS

There were 3 dropouts, two of whom relocated to a different town, and the third, who gave no specific reason. No adverse side effects were reported.

Effect of IGOB131 and Dyglomera™ on Body weight

Overweight participants who received either IGOB131 or Dyglomera (300mg daily) for 8 weeks had significantly ($p<0.05$) greater reduction in body weight compared to those on placebo (Table 1a). This reduction in body weight corresponded to a 9-10% reduction in BMI (Table 1b).

Table 1 a: The effect of IGOB131 and Dyglomera™ on body weight (kg)

	T0	T4	T8	Variation (%)
Placebo	73.51 ± 1.08^{a}	72.76 ± 1.28^{a}	72.26 ± 1.25^{a}	-1.74 ± 0.38^{a}
Test IGOB	74.07 ± 0.85^{a}	70.25 ± 0.90^{a}	66.66 ± 0.89^{b}	-10.00 ± 0.58^{b}
Test Dyglo	70.56 ± 0.83^{a}	67.42 ± 1.19^{b}	64.28 ± 1.09^{b}	-8.92 ± 0.80^{b}

Values are means ± sem

There was a slight but insignificant decrease in weight and BMI for participants taking placebo over the 8 -week test period.

Table 1b: The effect of IGOB131 and Dyglomera™ on BMI (kg/m^2)

	T0	T4	T8	Variation (%)
Placebo	27.58 ± 0.60^{a}	27.27 ± 0.56^{a}	27.08 ± 0.59^{a}	-1.74 ± 0.38^{a}
Test IGOB	27.31 ± 0.51^{a}	25.89 ± 0.48^{a}	24.58 ± 0.48^{b}	-10.00 ± 0.58^{b}
Test Dyglo	26.67 ± 1.84^{a}	25.45 ± 0.50^{b}	24.30 ± 0.63^{b}	-8.92 ± 0.80^{b}

Values are means ± sem

Body weight, BMI, % body fat, and waist-to- hip circumferences were slightly (1.3%, 0.8 cm, 2.0 cm respectively) reduced in the placebo group over the 8 week trial period. However,

IGOB131, as well as Dyglomera™, brought about a more significant reduction in these parameters (Tables 1c, 1d and 1e).

Table 1c: The effect of IGOB131 and Dyglomera™ on body fat (%)

	T0	T4	T8	Variation (%)
Placebo	37.4 ± 2.4^a	37.2 ± 1.5^a	36.1 ± 1.6^a	-1.3 ± 0.2^a
Test IGOB	36.8 ± 1.4^a	34.9 ± 2.3^b	31.7 ± 1.8^b	-5.1 ± 0.3^b
Test Dyglo	37.6 ± 2.8^a	35.3 ± 1.5^b	32.3 ± 1.5^b	-5.3 ± 0.5^b

Values are means ± sem.

Table 1d: The effect of IGOB131 and Dyglomera™ on waist circumference (cm)

	T0	T4	T8	Variation (%)
Placebo	87.6 ± 2.5^a	87.2 ± 1.7^a	86.8 ± 1.8^a	-0.8 ± 0.3^a
Test IGOB	86.3 ± 2.3^a	84.9 ± 2.3^a	83.2 ± 1.6^b	-3.1 ± 0.3^b
Test Dyglo	86.8 ± 1.8^a	85.1 ± 1.6^b	83.1 ± 1.3^b	-3.7 ± 0.6^b

Values are means ± sem.

Table 1e: The effect of IGOB131 and Dyglomera™ on hip circumference (cm)

	T0	T4	T8	Variation (%)
Placebo	92.8 ± 2.6^a	91.7 ± 2.4^a	90.8 ± 2.3^a	-2.0 ± 0.4^a
Test IGOB	91.6 ± 3.1^a	87.8 ± 3.3^a	85.3 ± 2.8^b	-6.3 ± 1.2^b
Test Dyglo	92.7 ± 2.4^a	90.3 ± 2.5^b	88.4 ± 0.6^b	-4.3 ± 1.3^b

Values are means ± sem.

Effect of IGOB131 and Dyglomera™ on Blood lipids

Eight-week use of IGOB131 by overweight participants reduced plasma total cholesterol by 10.5%, LDL-cholesterol by 24.7%, and triacylglycerol by 12.2%. This treatment also increased the concentration of HDL-cholesterol by 12.1% (Tables 2, 3, 4). A similar change in these parameters was observed in the Dyglomera™ group; 8.45% for total cholesterol, 17.27% for LDL-cholesterol and 14.30% for triglycerides. There was also a 13.36% increase in HDL-cholesterol.

Table 2: The effect of IGOB131 and Dyglomera™ on total cholesterol (mg/dL)

	T0	T4	T8	Variation (%)
Placebo	187.81 ± 2.75^a	186.28 ± 3.04^a	183.13 ± 2.82^a	-2.20 ± 0.36^a
Test IGOB	186.53 ± 2.63^a	174.64 ± 2.48^b	166.76 ± 2.42^b	-10.50 ± 0.85^b
Test Dyglo	190.72 ± 2.47^a	181.09 ± 2.65^a	174.56 ± 3.13^a	-8.45 ± 1.32^b

Values are means ± sem.

Table 3: The effect of IGOB131 and Dyglomera™ on triglycerides (mg/dL)

	T0	T4	T8	Variation (%)
Placebo	61.94 ± 2.41[a]	59.76 ± 2.16[a]	58.19 ± 2.82[a]	-5.75 ± 1.57[a]
Test IGOB	56.55 ± 2.42[a]	52.00 ± 2.06[b]	49.53 ± 2.08[b]	-12.20 ± 1.13[b]
Test Dyglo	58.63 ± 2.52[a]	52.76 ± 1.98[b]	50.40 ± 1.74[b]	-14.30 ± 1.55[b]

Values are means ± sem.

Table 4: The effect of IGOB131 and Dyglomera™ on LDL-cholesterol (mg/dL)

	T0	T4	T8	Variation (%)
Placebo	108.64 ± 2.78[a]	107.30 ± 3.16[a]	103.40 ± 2.82[a]	-4.85 ± 0.87[a]
Test IGOB	106.40 ± 3.29[a]	90.45 ± 3.10[b]	80.05 ± 2.97[b]	-24.76 ± 1.29[b]
Test Dyglo	123.00 ± 4.04[b]	110.76 ± 2.84[a]	101.43 ± 3.04[a]	-17.27 ± 1.82[b]

Values are means ± sem.

Over the 8-week test period, the circulating levels of HDL-cholesterol were also significantly increased ($p<0.05$) by Dyglomera™, as well as IGOB131 (Table 5).

Table 5: The effect of IGOB131 and Dyglomera™ on HDL-cholesterol (mg/dL)

	T0	T4	T8	Variation (%)
Placebo	66.78 ± 1.38[a]	67.02 ± 1.48[a]	68.09 ± 1.45[a]	1.98 ± 0.69[a]
Test IGOB	68.81 ± 1.12[a]	73.79 ± 1.00[b]	76.80 ± 0.81[b]	12.06 ± 1.59[b]
Test Dyglo	63.12 ± 2.57[a]	59.77 ± 2.65[b]	55.99 ± 2.73[b]	13.36 ± 2.26[b]

Values are means ± sem.

DISCUSSION

Results demonstrated that the extracts at a dose of 300 mg per day, were effective in significantly reducing weight, BMI, body fat, waist circumference, and hip circumference. IGOB131 and Dyglomera™ also positively modified lipid parameters in healthy overweight participants. These findings are superior to the majority of other randomized double-blind placebo-controlled clinical trials evaluating medicinal plant extracts, herbs and spices. For example, recently, an 8-week study carried out on 78 overweight subjects with *Cuminum cyminum* L. and Orlistat 120, showed significant decreases in weight (-1.1 ± 1.2 and -0.9 ± 1.5 vs. 0.2 ± 1.5 kg, respectively, $p = 0.002$) and BMI (-0.4 ± 0.5 and -0.4 ± 0.6 vs. 0.1 ± 0.6 kg/m^2, respectively, $p = 0.003$), in addition to beneficial effects on insulin metabolism compared with placebo [3]. Comparing those results to our study, the reduction in weight observed is nine times higher with IGOB131 and eight times higher with Dyglomera™ than *C. cyminum*. IGOB131 and Dyglomera™ reduced BMI 25 times and 22 times respectively, more effective than *C. cyminum* in overweight subjects and maintaining participants within a healthy BMI bracket.

The activity of plant extracts can be explained through the action some of their components have on body-fat metabolism and oxidation or increasing metabolic rate [1]. This has been

demonstrated in trials with epigallocatechin-3-gallate of green tea, virgin olive oil, and *Lycium barbarum* causing higher fat oxidation in human. The compounds may act by activating lipid metabolism, acceleration of oxidation, suppression of fatty acid synthesis and PPARc agonistic activity in overweight individuals, as well as in obese patients.

IGOB131 and Dyglomera™ have previously proven their activities with overweight and/or obese volunteers (defined as BMI > 25 kg/m^2). In a previous study [4] on 102 healthy overweight and obese participants who were administered a dose of 150 mg twice daily before meals, there were significant improvements in body weight, body fat, and waist circumference, as well as plasma total cholesterol, LDL cholesterol, blood glucose, C-reactive protein, adiponectin and leptin levels compared to a placebo group. IGOB131 was also very active in overweight participants in this study. In both obese and overweight groups, IGOB131 activity was attributed to the ability of the extracts to favorably impact adipogenesis through a variety of critical metabolic pathways, including PPAR gamma, leptin, adiponectin, and glycerol-3 phosphate dehydrogenase [5]. Furthermore, compared to the placebo group, the obese group treated with Dyglomera™ demonstrated a significant average weight reduction of 11.15 kg (-11.33% of total body weight) ($p < 0.001$) after 8 weeks of treatment (Table 1a). This reduction in weight was accompanied by a loss of visceral fat, as measured by waist circumference and lipid profiles [6]. The same trend was observed with overweight participants (Tables 2, 3, 4, 5).

The present study clearly demonstrates that administration of IGOB131 and Dyglomera™ can be used to prevent and manage weight increase, specifically targeting to limit the progression to obesity and the myriad of its complications. The antioxidant properties of both extracts have been intensively documented, and are suggested to be involved with curative activity [7]. However, there are only a few and controversial studies on oxidative stress in overweight subjects compared to obesity studies [8]. For example, one study demonstrated that oxidative stress increases with increasing BMI and age, as a sequel to an impaired antioxidant status, in addition to an increase of peroxides and uric acid and a disadvantaged lipid profile in overweight subjects. In contrast, another study [9] demonstrated that oxidative stress is not involved in the overweight status. However, it is established that lipid peroxidation is associated with several indices of adiposity and a low systemic antioxidant defense (i.e. antioxidant enzymes, tissue dietary antioxidants, glutathione [10], and leading to oxidative stress. In fact, in stress conditions ROS levels increase; because of their high reactivity, they are involved in cell damage, necrosis, and apoptosis, via oxidation of lipids, proteins, and DNA, in addition to provoking an endothelial dysfunction, infiltration, and activation of inflammatory cells [11]. The anti-oxidant property of the IGOB131 used in this study can be attributed to the presence of ellagic acid (EA). This polyphenolic compound has been shown to be antiproliferative and anti-inflammatory [12, 13]. Additionally, its efficacy in the management of obesity and metabolic syndrome has previously been reported [6].

The present study has also proven the capacity of these extracts to reduce body fat (Table 1c), waist and hip circumferences (Tables 1d and 1e respectively), total cholesterol (Table 2), triglyceride (Table 3), and LDL cholesterol levels (Table 4) in overweight participants. The observed reduction may be due to the presence of EA in IGOB131. In fact, lipid accumulation both in adipose tissue and liver are associated with increasing weight; progression to an overweight condition [13] and changes in weight are partially due to the metabolic reactions and

differentiation occurring in the adipose tissue. This can explain hypertrophy and hyperplastic expansion of adipocytes associated with being overweight and obese. Furthermore, EA has a lipid-lowering dietary compound; its inhibitory effects on adipogenesis seem to be associated, at least partly, with epigenetic modification. EA decreases hepatic lipid accumulation by targeting multiple mechanisms including FFA synthesis, TG sterification and FFA oxidation. In a recent study [12], there was evidence that EA plays separate, differing roles in manipulating excess lipid in adipocytes and hepatocytes, resulting in a synergistic attenuation the progression from overweight state to obesity and hepatic steatosis. EA also exerted the distinctive lipid-lowering properties to decrease biosynthesis of FA in both adipocytes and hepatocytes, but augmented FA oxidation only in hepatocytes. The presence of EA in extracts has also been shown to be effective in reducing atherosclerotic lesions and increasing cholesterol efflux in macrophages. Additionally, constituents of IGOB131 and Dyglomera including EA, may act via modulation of the expression of PPAR- gamma required for maintenance of the differentiated state of adipocytes, which has been reported to be involved in lipid accumulation and decreased expression of adipocyte markers. Several other transcription factors are likely to play an important role in the molecular control of adipogenesis like C/EBPs [14]. The presence of albumin in IGOB131 extracts may also contribute to the activity observed, although the function is not well understood. Albumin has been demonstrated to bind reversibly to many endogenous molecules (e.g., fatty acids), as well as pharmacologic agents [15]. It is speculated that this combination to other constituents can play a much more important role in buffering against sudden changes in absorption, thereby providing more consistent blood levels, similar to like detemir, an insulin preparation [16]. Albumin may also contribute to prolonged duration of action caused by some of the active compounds in our extracts. Other studies proved that the addition of molecules like albumin, a soluble 66.5 kD monomeric, leads to significant improvement in the solubility of the poorly soluble compounds [17. 18]. Another explanation for the role of albumin in weight reduction and lipid profile can be described from its presence in Whey protein. In fact, the presence of albumin in whey, a dietary protein which stimulates energy expenditure, has a greater thermogenic effect in the postprandial period compared to carbohydrates and fats, and additionally decreases energy intake through mechanisms that influence appetite. Whey amino acids on insulin secretion, incretin hormones released from the gut, also seem to be involved, in particular gastric inhibitory peptide (GIP) and glucagon-like peptide 1 (GLP-1). Furthermore, the presence of albumin in our extracts could influence absorption process at the intestinal level, considering that the postprandial rate of protein synthesis also depends on the speed of protein absorption and that fast absorbing protein has an anabolic effect [19].

Abbreviations Used: GLP1, glucagon-like peptide; GIP, gastric inhibitory peptide; BMI, body mass index; FFA, free fatty acids; TG, triglyceride; PPAR, peroxisome proliferator-activated receptors; EA; ellagic acid; ROS, reactive oxygen species; LDL, low density lipoprotein; HDL, high density lipoprotein ; DG, Dyglomera™, extract of *Dichrostachys glomerata*; IGOB131, extract of *Irvingia gabonensis*.

Competing Interests: The authors have no financial interests or conflicts of interest.

Authors' Contributions: All authors contributed to this study.

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