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ORIGINAL ARTICLE

Possible Alterations of Changes in Weight, Appetite and Reproductive Biomarkers of Female Wistar Rats Using Blends of Cucumber, Green Tea and Orlistat®

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ABSTRACT

Anti-obesity interventions, including orlistat and plant-derived products such as cucumber (*Cucumis sativus*) and green tea (*Camellia sinensis*), promote weight reduction through mechanisms such as inhibition of digestive enzymes, appetite suppression, and reduced fat absorption. Despite their widespread use, information on their physiological and reproductive effects, particularly when administered in combination, remains limited. This study investigated the effects of orlistat (O), cucumber extract (C), green tea extract (G), and their combinations (C+O and G+O) on appetite regulation, body weight, lipid profile, and reproductive hormones in female Wistar rats. Specifically, the study aimed to investigate the effects of administering cucumber extract (C), green tea extract (G), orlistat (O), cucumber-orlistat (C+O), and green tea-orlistat (G+O) on: (i) serum leptin concentration; (ii) feed intake and body weight; (iii) serum cholesterol and triglyceride concentrations; and (iv) reproductive hormones (progesterone and follicle-stimulating hormone [FSH]) and the relationships among treatment, body mass index (BMI), estrogen, leptin, progesterone, and FSH in female Wistar rats. Data were analyzed using R. Cucumber-treated rats exhibited the lowest body weight, feed intake, and serum cholesterol, whereas both cucumber and green tea treatments reduced serum triglyceride concentrations. The highest leptin concentrations were observed in the cucumber and cucumber-orlistat groups, while progesterone was highest in the green tea-orlistat group, estrogen in the orlistat group, and FSH in the cucumber and cucumber-orlistat groups. Statistical analyses revealed that treatment significantly affected leptin concentrations, body weight and feed intake, lipid profile, and reproductive hormones. Furthermore, estrogen, BMI, treatment, and the period of administration significantly explained variation in body weight, leptin, FSH, and progesterone. Principal component analysis showed that body weight was positively associated with serum triglycerides but inversely associated with leptin, while leptin was negatively associated with serum cholesterol and feed intake. Overall, cucumber extract, either alone or in combination with orlistat, showed the greatest potential for improving body weight regulation while enhancing leptin and reproductive hormone concentrations. However, withdrawal of treatment was associated with a marked rebound in body weight, suggesting that the beneficial effects may not be sustained after discontinuation.

Keywords: Leptin; Cucumber; Orlistat; Green tea leaves; Reproductive hormones; Obesity.

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1.0 INTRODUCTION

Maintaining a healthy body weight through regular exercise, balanced dietary practices, and appropriate pharmacological interventions reduces the risk of chronic diseases and improves overall health outcomes (Hauner et al., 2011). Consequently, increasing attention has been directed toward weight management interventions, including natural products such as cucumber (*Cucumis sativus* L.) and green tea (*Camellia sinensis* L.), as well as commercially available drugs such as Orlistat. Cucumber is low calorie food rich in dietary fiber, which may enhance satiety, improve digestion, and reduce appetite (Akhtar et al., 2020). Green tea contains bioactive compounds, particularly caffeine and catechins, which have been reported to enhance energy expenditure, stimulate fat oxidation, and increase metabolic rate (NHMRC, 2013; Williams et al., 2013). In contrast, Orlistat acts primarily by inhibiting gastrointestinal lipases, thereby reducing the hydrolysis and absorption of dietary triglycerides and limiting intestinal uptake of free fatty acids and monoglycerides (Zhi et al., 1995). However, prolonged inhibition of fat absorption may interfere with the uptake of fat soluble vitamins, including vitamins A, D, E, and K (Jain et al., 2011). Although these interventions are widely used for weight management, evidence suggests that they may also influence other physiological processes. Green tea consumption has been associated with alterations in reproductive health indices (Kao et al., 2000; Adani et al., 2013; Das and Karmakar, 2015), whereas Orlistat use has been linked to gastrointestinal complications, including abdominal discomfort and anal fissures (Hanefeld and Sachse, 2002; Torgerson et al., 2004; O'Meara et al., 2004). Despite increasing interest in their weight reducing effects, investigations into their broader metabolic, cardiovascular, and reproductive consequences remain limited (Khan et al., 2012). Previous

studies have largely focused on their efficacy in reducing body weight and improving metabolic outcomes (Mak, 2012; Suzuki et al., 2016; Yang et al., 2016; Pervin et al., 2018; Musial et al., 2020). The limited understanding of the physiological consequences of combining natural and pharmacological weight management interventions represents an important knowledge gap. Consumers frequently combine plant based products with commercially available weight loss medications with the expectation of enhanced effects; however, such combinations may produce unpredictable interactions affecting lipid metabolism, appetite regulation, and endocrine function. This concern is supported by reports from the Food and Drug Administration highlighting potential adverse effects associated with prolonged Orlistat use, including hepatotoxicity, acute pancreatitis, gallstones, and renal failure (George et al., 2020). Similarly, comparatively few studies have examined the potential effects of green tea on reproductive and cardiovascular health parameters (Khan et al., 2012; Das & Karmakar, 2015). Wistar rats are widely used in biomedical research because of their manageable size, high reproductive capacity, dietary adaptability, and established application in nutritional, toxicological, and pharmacological studies (National Research Council, 1995; Delwatta et al., 2018). They have also been extensively employed for investigating drug safety, disease mechanisms, and physiological responses to chemical interventions (Andong et al., 2021).

Therefore, this study aimed to evaluate the effects of cucumber extract, green tea extract, Orlistat, and their combinations on appetite regulation, body weight, lipid profile, and reproductive hormones in female Wistar rats. Specifically, the study investigated the effects of these interventions on: (i) serum leptin concentration; (ii) feed intake and body weight; (iii) serum cholesterol and triglyceride concentrations; and (iv) reproductive hormones, including progesterone and follicle stimulating hormone (FSH), as well as the relationships among treatment, body mass index (BMI), estrogen, leptin, progesterone, and FSH.

2.0 MATERIALS AND METHODS

2.1 Study design

This study lasted for 2 months, coinciding with the female rats' estrus period (usually 4-5 days from 8-12 weeks of age) (Marcondes et al., 2002). It was also in line with the procedures of the National Institute of health Guide for the Care and Use of Laboratory Animals (National Research Council, 1995; National Research Council, 2011).

2.2 Sample preparation

Fresh cucumber (*Cucumis sativus* L.) fruits and green tea (*Camellia sinensis* L.) leaves were thoroughly rinsed with distilled water, cut into small pieces, shade dried to constant weight, and milled into fine powder using a JAICO® laboratory blender. The powdered samples were separately extracted with distilled water at a ratio of 1:100 (w/v) by maceration for 24 h at room temperature with intermittent stirring (Oboh et al., 2017). The mixtures were filtered (HAVER® EML 200 Digital Plus filtration system) to obtain the aqueous extracts, which were prepared fresh before oral administration. For the standard treatment, the contents of one Orlistat® capsule (120 mg) were suspended in 10 mL of distilled water to obtain a stock suspension of 12 mg/mL. The suspension was mixed thoroughly before each administration to ensure uniform dispersion of the drug, and the required volume was administered orally according to the body weight of each rat.

2.3 Ethical consideration

Ethical approval for this study was granted by the Health Research Ethics Committee of the University of Nigeria, Nsukka, with institutional permission secured from Enugu State University of Science and Technology Teaching Hospital for data collection.

2.4 Sample collection and authentication

They were provided with high fat rat chow and water *ad libitum* throughout the acclimatization period. Fresh green tea (*Camellia sinensis* L.) leaves were obtained from the vegetatively propagated fields of the Cocoa Research Institute of Nigeria (CRIN) Substation, Kusuku, Mambilla, Taraba State, Nigeria. Fresh cucumber (*Cucumis sativus* L.) fruits were purchased from Ogige Market, Nsukka, while Orlistat capsules (120 mg) were obtained from a pharmaceutical shop in Nsukka, Enugu State, Nigeria (6°51′24″N, 7°23′45″E). The cucumber and green tea samples were authenticated by Dr. Felix Nwafor of the Department of Plant Science and Biotechnology, University of Nigeria, Nsukka, before use in the study.

2.5 Experimental animals

Female Wistar rats (n = 20), weighing approximately 68 g, were obtained from the Animal House of the Department of Zoology and Environmental Biology, University of Nigeria, Nsukka. The rats were acclimatized for 12 days under standard laboratory conditions at a room temperature of approximately 25 ± 2 °C with a 12 h light:12 h dark photoperiod.

2.6 Experimental design

The aqueous cucumber and green tea extracts were lyophilized to obtain stable dry extracts for accurate dose preparation. Before administration, the lyophilized extracts were reconstituted in distilled water to the required concentrations. Orlistat® was not lyophilized because it was supplied as a commercially formulated capsule. Instead, the contents of one 120 mg capsule were suspended in 10 mL of distilled water to prepare a stock suspension (12 mg/mL), which was thoroughly mixed before each administration to ensure uniform dispersion. The daily dose for each rat was calculated based on its body weight using the formula: Dose (mg) = prescribed dose (mg/kg body weight) × body weight (kg). The calculated dose was then divided by the concentration of the prepared suspension or extract (mg/mL) to obtain the volume (mL) required for oral gavage each day.

Following acclimatization, the rats were randomly assigned to six experimental groups, with three biological replicates (three rats) per group (n = 3; total = 18 rats). Each rat was housed individually in a separate cage to prevent competition for feed and to allow accurate measurement of individual feed intake throughout the study. No technical replicates were used in the experimental design; each animal represented one independent experimental unit.

The treatment groups were as follows:

Group 1 (Control): 100 g of feed and water only.
Group 2 (Cucumber): 100 g of feed, water, and 2 mL cucumber extract.
Group 3 (Green tea): 100 g of feed, water, and 2 mL green tea extract.
Group 4 (Orlistat): 100 g of feed, water, and 2 mL Orlistat suspension.
Group 5 (Cucumber + Orlistat): 100 g of feed, water, 1 mL cucumber extract, and 1 mL Orlistat suspension.
Group 6 (Green tea + Orlistat): 100 g of feed, water, 1 mL green tea extract, and 1 mL Orlistat suspension.

2.7 Assessing feed consumption

At the end of each 24 h feeding period, the amount of feed remaining in the feeding tray and the quantity of feed spilled onto plastic sheets placed beneath each cage were collected and weighed. Daily feed intake for each rat was calculated using the following equation:

Feed intake (g/day) = Initial feed provided (g) − [Feed remaining in the tray (g) + Feed spilled (g)]

An initial quantity of 100 g of feed was provided to each rat daily, and the calculated feed intake was used for subsequent statistical analyses.

2.8 Assessing body weight and size

Body mass and body length of each rat were measured three times per week before the morning feeding throughout the experimental period. Body mass was determined using a calibrated digital balance, whereas body length was measured with a flexible measuring tape from the tip of the nose to the base of the tail while the animal was gently restrained. Body condition was estimated from the relationship between body mass and body length using linear regression analysis, with the residual values serving as an index of body condition.

2.9 Blood collection

Baseline blood collection was conducted on the first day of extracts administration. Collection site was the tail region, which was first sterilized with 70% alcohol and punctured with a sterilized lancet before blood drawn into heparinized and unheparinized micro hematocrit capillary tubes (within 2 minutes of restraint to avoid any physiologic changes in samples) (Romero & Reed 2005; Elabarany 2018; Pouadjeu et al. 2023). Blood in plain capillary tubes was slanted at room temperature for 15-30 minutes (to initiate the clotting process and separate serum from the blood) before being centrifuged at 3000 rpm for 10 minutes. The samples were stored at -20 ºC in a refrigerator before hormonal assay (leptin, progesterone, estrogen, and follicle stimulating hormone). Blood from heparinized tubes, on the other hand, was used to measure serum triglycerides and cholesterol levels. All blood samples were collected weekly for 12 weeks.

2.10 Serum cholesterol and triglyceride analysis
Serum total cholesterol and triglyceride concentrations were determined using a CardioChek® point of care analyzer according to the manufacturer's instructions and the procedure described by Morales et al. (2020). Blood samples were collected from each rat, and the serum was analyzed immediately following separation to determine total cholesterol and triglyceride concentrations.

2.11 Total fecal triglyceride analysis
Total fecal triglyceride content was determined using a modified Soxhlet extraction method as previously described (Thiex et al., 2003; Hopkins et al., 2014; Holman et al., 2019; Navratilova et al., 2020; Posridee et al., 2023). Briefly, fecal samples were oven dried to constant weight, ground into a fine powder, and homogenized. Approximately 2 g of each dried fecal sample was transferred into an extraction thimble and extracted with 85 mL of hexane for 3 h using a Soxhlet extraction apparatus. Following extraction, the solvent was evaporated, and the extracted samples were dried in an oven to remove residual solvent. Total fecal triglyceride content was determined gravimetrically by calculating the difference in sample weight before and after extraction and was expressed as a percentage of the fresh (wet) fecal sample weight (Thiex et al., 2003; Holman et al., 2019).

2.12 Hormonal analysis
Serum concentrations of leptin, progesterone, estrogen, and follicle stimulating hormone (FSH) were determined using enzyme linked immunosorbent assay (ELISA) kits according to the manufacturers' instructions. Serum leptin was quantified using a Sandwich ELISA kit (Cat. No. ABIN6957435; Limerick, PA, USA). Serum progesterone (Cat. No. 55-PROMS-E01), follicle stimulating hormone (FSH; Cat. No. 11-FSHHU-E01), and estrogen (Cat. No. 55-ESTRT-E01) were quantified using ALPCO® mouse/rat ELISA kits specific for each hormone. All samples and standards were analyzed in accordance with the manufacturers' protocols. The intra assay coefficient of variation (CV) obtained in this study was within the manufacturers' specified limit of ≤ 5% (Turner et al., 2022). Absorbance was measured at 450 nm using a Thermo Fisher Scientific® microplate reader (Fisher Scientific, Porto Salvado, Portugal), and hormone concentrations were calculated from the corresponding standard curves (Andong et al., 2024).

2.13 Data analysis
Data were analyzed using R software version 3.2.5 (R Development Core Team, 2021; Andong et al., 2023). Data normality was assessed using the Shapiro Wilk test, while homogeneity of variances was evaluated using Levene's test before conducting parametric analyses. One way ANOVA was used to determine the effects of extract treatments and administration periods on serum leptin concentrations, followed by Tukey's honestly significant difference (HSD) test for pairwise comparisons. Multivariate analysis of covariance (MANCOVA) was applied to evaluate the effects of extracts and leptin on feed intake and body weight, while controlling for covariates. MANOVA was used to assess the influence of extracts and administration periods on lipid profiles and reproductive hormones, including cholesterol, triglycerides, progesterone, and follicle stimulating hormone (FSH). Principal component analysis (PCA) was performed to identify relationships among treatments, body condition, lipid variables, leptin, and reproductive hormones. Statistical significance was set at $P < 0.05$.

3.0 RESULTS

The control group had a higher mean weight and size (113.1 ± 0.1 and 165.8 ± 1.1), while the cucumber and its combination with orlistat group experience the least weight (85.40 ± 0.5 and 86.00 ± 0.5) than the other treated groups. The control group also consumed more feed (95.20 ± 0.6), while the cucumber extract group consumed the least (36.60 ± 0.3). The control group had lower level of leptin and progesterone (0.19 ± 0.8 and 1.99 ± 0.2), while combination of cucumber, orlistat and green tea leaves had the highest concentration of leptin and progesterone (0.69 ± 0.3 and 3.02 ± 0.0) (Table 1). The control group also had a higher mean cholesterol level (53.50 ± 0.0), while the cucumber treated group accumulated the least (29.50 ± 0.8). Fecal triglyceride was higher in green tea and orlistat groups (21.40 ± 0.6 and 20.80 ± 0.1). However, blood triglyceride was higher in the control group (48.50 ± 0.3), and found to be lowest in green tea and cucumber treated groups (28.30 ± 0.3 and 29.70 ± 0.0). For estrogen, it was higher in the control and orlistat treated groups (20.94 ± 0.0 and 19.92 ± 0.1), while FSH was more in the cucumber extract and the extract combining cucumber and orlistat (23.78 ± 0.0 and 23.27 ± 0.1) (Table 1). Different types of extracts correlated significantly with leptin ($p < 0.04$), while the period of administration did not ($p < 0.28$). Conversely, in a joint interactive effect, leptin concentration correlated with both types of extracts at different period of administration ($p < 0.01$) (Table 2). In pairwise analyses, cucumber extract correlated significantly to the extract combination cucumber and orlistat ($p < 0.05$) and the control group ($p < 0.01$). In turn, the control group correlated significantly with the extract of green tea ($p < 0.01$), orlistat ($p < 0.01$), and the extract combination of cucumber and orlistat ($p < 0.01$), green tea and orlistat groups ($p < 0.01$). The blend of green tea leaves and orlistat correlated significantly with orlistat extract ($p < 0.05$) (Table 3).

Table **1**. Information of the high fat feed formulation for rodents

	Amount (Kg)	Amount (%)	Energy value per 100 g (Kcal)
Maize	2.75	17.67	0.125
Wheat offal	0.25	1.61	0.104
Fish meal	0.50	3.21	0.444
Groundnut cake	2.75	17.67	0.105
Animal fat (lard)	-6.25	40.16	0.896
Palm kernel cake	2.5	16.06	0.862
Bone meal	0.25	1.16	0
Methionine	0.125	0.80	0
Lysine	0.125	0.80	0
common salt	0.031	0.20	0
Vitamin premix	0.031	0.20	0

Table **2**. Mean feed consumption, weight, size, leptin, cholesterol, triglyceride and hormones of treated female Wistar rats

Variables	Control	G	C	O	C + O	G + O
Weight (g)	113.1 ± 0.1	89.80 ± 0.7	85.40 ± 0.5	88.30 ± 0.0	86.00 ± 0.5	87.90 ± 0.1
Size (m)	165.8 ± 1.1	145.0 ± 0.0	143.3 ± 0.1	147.9 ± 0.0	145.4 ± 0.0	147.3 ± 0.1
Leptin (µg/dL)	0.19 ± 0.8	0.44 ± 0.0	0.62 ± 0.3	0.45 ± 0.0	0.69 ± 0.3	0.41 ± 0.0
Cholesterol (mg/dL)	53.50 ± 0.0	37.50 ± 0.0	29.50 ± 0.8	38.40 ± 0.3	37.40 ± 0.1	35.90 ± 0.4
Fecal triglyceride (mg/dL)	15.90 ± 0.4	21.40 ± 0.6	13.60 ± 0.7	20.80 ± 0.1	16.8 ± 0.2	19.20 ± 0.0
Blood triglyceride (mg/dL)	48.50 ± 0.3	28.30 ± 0.3	29.70 ± 0.0	29.30 ± 0.5	31.30 ± 0.2	31.90 ± 0.5
Progesterone (µg/dL)	1.99 ± 0.2	2.62 ± 0.5	3.13 ± 0.5	2.62 ± 0.1	2.79 ± 0.0	3.02 ± 0.0
Estrogen (µg/dL)	20.94 ± 0.0	19.72 ± 0.1	19.75 ± 0.2	19.92 ± 0.1	19.63 ± 0.3	19.80 ± 0.6
FSH (µg/dL)	21.98 ± 0.0	22.42 ± 0.4	23.78 ± 0.0	21.59 ± 0.1	23.27 ± 0.1	21.33 ± 0.1
Feed consumption (kcal)	95.20 ± 0.6	42.90 ± 0.0	36.60 ± 0.3	41.30 ± 0.0	41.80 ± 0.0	47.5 ± 0.1

Cucumber (C), green tea leaves (G) and orlistat (O).

Table **3**. Factorial analyses of extracts and period administration in relation to leptin concentration.

Variables	Sum Sq	Mean Sq	F	p
Leptin				
Period	0.02	0.01	1.32	0.28
Extracts	0.38	0.08	45.1	0.04
Period × Extracts	0.05	0.01	4.11	0.01

In MANCOVA, body weight and feed consumption indicated a significant correlation with the different types of extracts ($p < 0.05$) (Table 4). In a pair wise analyses, the blend of orlistat and cucumber, and green tea and orlistat groups significantly correlated with body weight ($p < 0.05$). Meanwhile, feed consumption significantly varied between control group

and the cucumber, orlistat, green tea, blend of cucumber and orlistat, cucumber and orlistat (Table 5).

Table **4**. Pair wised Tukey's HSD for extracts and leptin concentration.

Variables			Estimate	SE	t	p
Leptin						
(C+O)	–	(C)	0.09	0.03	3.16	0.03
(C)	–	Control	0.25	0.03	8.90	0.01
(G)	–	(C)	0.03	0.03	1.09	0.88
(G+O)	–	(C)	0.05	0.03	1.71	0.53
(O)	–	(C)	0.05	0.03	1.85	0.44
(C+O)	–	Control	0.16	0.03	5.74	0.01
(G)	–	(C+O)	-0.06	0.03	-2.07	0.32
(G+O)	–	(C+O)	-0.04	0.03	-1.45	0.69
(O)	–	(C+O)	-0.04	0.03	-1.31	0.78
(G)	–	Control	-0.22	0.03	-7.81	0.01
(G+O)	–	Control	-0.20	0.03	-7.19	0.01
(O)	–	Control	-0.19	0.03	-7.05	0.01
(G+O)	–	(G)	0.02	0.03	0.62	0.99
(O)	–	(G)	0.02	0.03	0.76	0.97
(O)	–	(G+O)	0.01	0.03	0.15	1.00

(O) = Orlistat, (G) = green tea leaves, (C) = cucumber

Table **5**. Analyses of variance for weight and feed consumption in relation to extracts. Only significant values are extracted.

Variables	Sum Sq	Mean Sq	F	p
a) Body weight				
Extracts	5577.3	1115.5	2.70	0.03
b) Feed consumption				
Extracts	24175.1	4835.0	38.0	0.01

In MANOVA, cholesterol, serum and blood triglycerides correlated significantly to extracts and period of administration ($p < 0.05$). However, we found that only serum cholesterol significantly correlated to the interaction between types of extracts and period of administration ($p < 0.02$) (Table 6). In pair wise analyses, fecal triglyceride of green tea and cucumber extracts significantly varied. While serum triglyceride and cholesterol of the rats treated with the different forms of extract correlated mostly with control group (Table 7).

Table **6**. Body weight and feed consumption in relation to extracts concentration.

Variables			Estimate	SE	*t*	*P*
a) Body weight						
(C+O)	–	Control	27.10	9.084	2.983	0.04
(G+O)	–	Control	-27.20	9.084	-2.994	0.04
b) Feed consumption						
(C)	–	Control	58.60	5.047	11.61	0.01
(C+O)	–	Control	53.40	5.047	10.58	0.01
(G)	–	Control	-52.30	5.047	-10.36	0.01
(G+O)	–	Control	-47.70	5.047	-9.451	0.01
(O)	–	Control	-53.90	5.047	-10.68	0.01

(O) = Orlistat, (G) = green tea leaves, (C) = cucumber. Pair wised Tukey's HSD

Table **7**. Analyses of variance for cholesterol, serum and fecal triglycerides in relation to extracts and period of administration

Variables	Sum Sq	Mean Sq	*F*	*P*
a) Serum triglyceride				
Extracts	2908.5	581.71	9.871	<0.001
Period	4974.8	1243.7	21.10	<0.001
Extracts × Period	1605.0	80.250	1.361	0.22
b) Fecal triglyceride				
Extracts	460.35	92.070	4.070	0.006
Period	381.43	95.358	4.216	0.007
Extracts × Period	626.57	31.328	1.385	0.205
a) Serum cholesterol				
Extracts	3147.4	629.48	13.2615	<0.001
Period	1504.4	376.11	7.9236	<0.001
Extracts × Period	2198.8	109.94	2.3161	0.02

The period of administration of extract indicated that fecal triglyceride and serum cholesterol significantly varied more during the first and post period of extract administration. While serum triglyceride also varied significantly ($p < 0.05$) by first and post period of administration, estrus and post period, second and post period, and third and post period of administration (Table 8).

Table **8**. Cholesterol, serum and fecal triglycerides in relation to extracts

Variables			Estimate	SE	*t*	*P*
a) Serum triglycerides						
(C)	–	Control	18.80	5.560	3.381	0.02
(C+O)	–	Control	17.20	5.560	3.093	0.04
(G)	–	Control	-20.20	5.560	-3.633	0.01
(G+O)	–	Control	-16.60	5.560	-2.985	0.04
(O)	–	Control	-19.20	5.560	-3.453	0.01
b) Fecal triglycerides						
(G)	–	(C)	7.800	2.499	3.121	0.03
c) Serum cholesterol						
(C)	–	Control	24.00	4.358	5.507	< 0.001
(C+O)	–	Control	16.10	4.358	3.695	0.006
(G)	–	Control	-16.00	4.358	-3.672	0.006
(G+O)	–	Control	-17.60	4.358	-4.039	0.002
(O)	–	Control	-15.10	4.358	-3.465	0.01

(O) = Orlistat, (G) = green tea leaves, (C) = cucumber. Pair wised Tukey's HSD

In MANOVA, progesterone correlated significantly with the extract, period of administration and the interaction between extracts and period of administration ($P < 0.05$), while and follicle stimulating hormone correlated with period and the interaction between extracts and period of administration ($p < 0.05$) (Table 9).

Table **9**. Pair wised Tukey's HSD for cholesterol, serum and fecal triglycerides in relation to period of administration

Variables			Estimate	SE	*t*	*P*
a) Serum triglycerides						
Estrus	–	Post	0.193	0.044	4.412	0.004
First	–	Post	2.317	0.044	5.310	<0.001
Second	–	Post	-0.235	0.044	-5.405	<0.001
Third	–	Post	- 0.331	0.044	-7.304	<0.001
b) Fecal triglycerides						
First	–	Post	-7.333	2.313	-3.171	0.02
c) Serum cholesterol						
First	–	Post	-15.50	4.529	-3.422	0.009

In MANCOVA, weight, leptin, follicle stimulating hormone and progesterone in relation to estrogen, body size and extracts, it was found that estrogen correlated significantly to follicle stimulating hormone, progesterone estrogen ($p < 0.05$). The different types of extract correlated significantly with body weight and leptin concentration ($p < 0.05$) (Table 10).

Table **10**. Progesterone and follicle stimulating hormone in relation to extracts and period of administration

Variables	Sum Sq	Mean Sq	*F*	*P*
Progesterone				
Period	162.10	40.53	113.06	<0.001
Extracts	8.05	1.61	4.49	0.004
Period × Extracts	27.01	1.35	3.77	<0.001
FSH				
Period	1024.08	256.02	31.56	<0.001
Extracts	46.44	9.29	1.15	0.36
Period × Extracts	609.64	30.48	3.76	<0.001

In PCA, weight (0.80), feed consumption (0.80), cholesterol (0.55) and blood triglyceride (0.83) contributed more to the first PC. While size (0.55), progesterone (0.69), estrogen (0.50) and follicle stimulating hormone (0.60) contributed more to the second PC (Table 11).

Table **11**. Weight, leptin, follicle stimulating hormone and progesterone in relation to estrogen, body size and extracts

Variables	Sum Sq	Mean Sq	*F*	*P*
FSH				
Estrogen	157.17	157.16	4.8617	0.03
Leptin				
Extracts	0.38	0.08	21.26	<0.001
Progesterone				
Estrogen	32.34	32.34	9.41	0.003
Weight				
Extracts	5577.3	1115.5	5.11	<0.001
Size	4216.5	4216.5	19.30	<0.001
Estrogen	1190.0	1190.0	5.45	0.023
Extracts × Size	6604.9	1321.0	6.05	<0.001

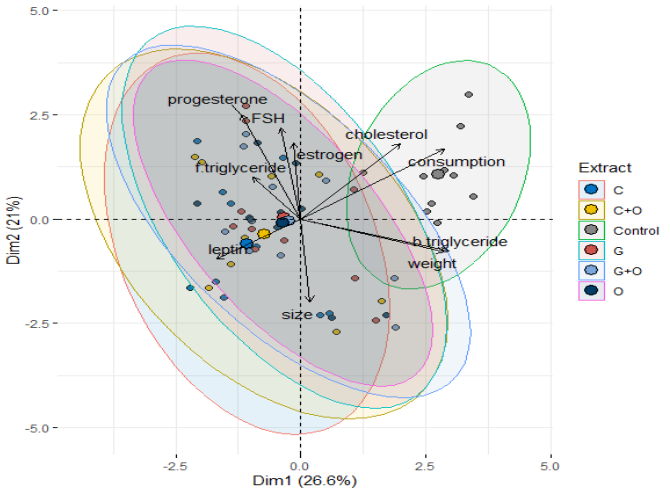

*Figure **1**: Principal component analyses (PCA) indicating the score plot for the first and second components. The smallest oval shape circled by green line indicates distribution of variables in the control group; the large oval shape circled by yellow line indicates distribution of variables in the blend of cucumber and orlistat extract group (C+O); large oval shape circled by red line indicates the cucumber extract group (C); the oval shape circled by light blue line indicates green tea leaves extract group (G); the oval shape circled by blue line indicates blend of green tea and orlistat extract group (G+O); the oval shape circled by pink line indicates orlistat extract group (O). The arrows of the PCA indicates approximation of variance of variables, and then their angles approximate the correlations. More so, points closer to each other usually signify that they have similar score on PCA components (n = 18 female rats).*

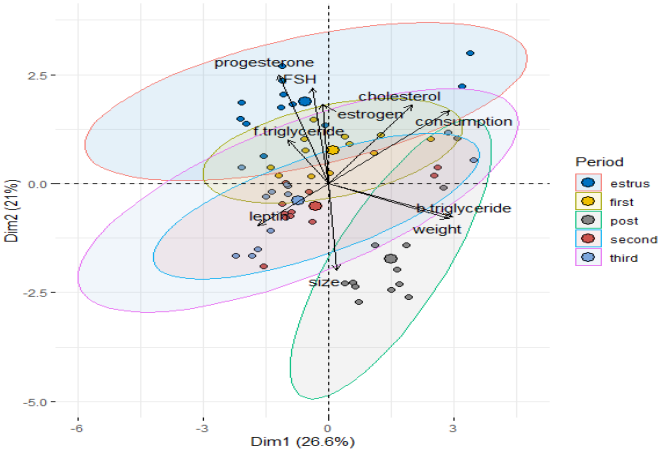

*Figure **2**. Principal component analyses (PCA) indicating the score plot for the first and second components. The smallest oval shape circled by yellow line indicates distribution of variables during the first period of extract administration; the smaller oval shape circled by blue line indicates distribution of variables during second period of extract administration; the larger oval shape circled by pink line indicates distribution of variables during third period of extract administration; the large oval shape circled by red line indicates distribution of variables during estrus period; the larger oval shape circled by green line is the post period of no extract administration. The arrows of the PCA indicates approximation of variance of the variables, and then their angles approximate the correlations. More so, points closer to each other usually signify that they have similar score on PCA components (n = 18 female rats).*

4.0 DISCUSSION

Obesity results from a persistent imbalance between energy intake and energy expenditure and remains a major global public health concern because of its association with metabolic disorders, including cardiovascular diseases and type 2 diabetes (Vangoori et al., 2022). Although pharmacological and plant-derived interventions are increasingly explored for weight management, their effectiveness depends not only on their ability to reduce body weight during administration but also on their influence on metabolic adaptation after treatment withdrawal. In the present study, cucumber extract, green tea extract, Orlistat, and their combinations influenced body condition, feed intake, and metabolic responses in female Wistar rats. The reduction in body weight observed in treated groups suggests that these interventions modified energy balance through different mechanisms involving appetite regulation, lipid metabolism, and nutrient absorption. However, the increase in body weight following discontinuation of treatment indicates a possible compensatory response, where restoration of normal metabolic activity and energy availability may promote weight regain. Similar rebound effects have been reported following cessation of weight management interventions, suggesting that sustained regulation of metabolic pathways may be necessary for maintaining long-term benefits (Verhaegen et al., 2019). Leptin concentration was significantly influenced by treatment type and by the interaction between treatment and duration of administration. This finding highlights the importance of leptin signalling in regulating energy homeostasis. Leptin, an adipocyte-derived hormone, communicates peripheral energy stores to the hypothalamus through leptin receptors (LepR), activating anorexigenic pathways that suppress appetite and regulate energy expenditure (Ahima & Flier, 2000; Allison & Myers, 2014; Friedman, 2019). The higher leptin response observed following cucumber supplementation and cucumber combined with Orlistat suggests that these treatments may have influenced appetite-related pathways. However, the response should be interpreted as altered leptin regulation rather than direct evidence of improved leptin sensitivity, because leptin concentration is influenced by adiposity, nutritional status, and metabolic condition. The potential role of cucumber extract in appetite regulation may be associated with its high dietary fibre content and bioactive compounds. Fibre increases satiety by delaying gastric emptying and promoting signals involved in appetite control. In addition, cucumber-derived triterpenoid saponins have been reported to inhibit pancreatic lipase activity, which may reduce lipid digestion and influence energy availability (Subandi et al., 2018). These mechanisms may explain the lower feed intake observed in cucumber-treated rats. Reduced energy consumption may subsequently contribute to improved weight regulation by limiting caloric availability and altering energy storage. The combined administration of cucumber extract and Orlistat produced responses consistent with the complementary actions of these interventions. While cucumber may influence satiety pathways through fibre and phytochemical-mediated mechanisms, Orlistat acts mainly by inhibiting gastrointestinal lipases, reducing triglyceride hydrolysis and limiting intestinal fatty acid absorption. Therefore, the combination may influence both energy intake and energy assimilation. Nevertheless, the increase in body weight observed during the post-treatment period (Figure 1) suggests that these effects may depend on continuous exposure to the interventions. Following withdrawal, restoration of normal digestive processes and energy availability may contribute to weight regain, emphasizing the need to consider metabolic adaptation when evaluating weight management strategies. The relationship among leptin, feed intake, and body weight further supports the role of endocrine regulation in energy balance. The inverse association between leptin and feed consumption suggests that increased leptin signalling may contribute to reduced appetite, whereas lower leptin levels may be associated with increased food intake and weight accumulation. However, the observed associations from multivariate analysis should not be interpreted as direct causal relationships because appetite regulation involves complex interactions among adipose tissue signals, nutritional status, and hormonal pathways.

Limitation

Study limitations should also be considered when interpreting these findings. Although the treatments influenced body weight, lipid metabolism, appetite-related responses, and reproductive hormones, obesity was not experimentally induced in the female Wistar rats. Therefore, the observed responses should be interpreted as effects on physiological weight regulation rather than definitive anti-obesity efficacy. The absence of an obesity-induced model limits direct extrapolation of these findings to obese conditions, where metabolic alterations may influence treatment responses differently. More so, the cucumber extract was not subjected to phytochemical characterization and quantification in the present study. Although previous studies have reported bioactive constituents associated with cucumber, the contribution of specific phytochemicals to the observed physiological responses cannot be confirmed from the current data. Future investigations incorporating obesity models and comprehensive phytochemical profiling would provide further insight into the mechanisms underlying these responses.

Conclusion

This study demonstrated that different weight management interventions produced distinct metabolic and reproductive responses in female Wistar rats. Cucumber extract, particularly when administered alone or combined with Orlistat, showed greater potential for weight regulation, which was associated with altered leptin responses and reduced feed intake. The findings suggest that cucumber-based interventions may influence energy balance through appetite-related pathways, while Orlistat may provide complementary effects through modulation of lipid absorption. However, the observed increase in body weight following treatment withdrawal indicates that the benefits of these interventions may not be sustained after discontinuation. Overall, the study highlights that natural and pharmacological weight management strategies can influence body condition, lipid metabolism, and hormonal regulation through interconnected metabolic pathways.

Data availability statement

Data will be made available on request.

Competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors contribution

Study was conceived by RAA, FAA; laboratory work by IN, RAA; drafting of manuscript by FAA; Statistical design and data analyses by FAA; manuscript revised and edited by RAA, IN, FAA. All authors approved submission for consideration

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