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Effect of 4-H Time Restricted Feeding on Body Weight, Leptin Concentration and Lipid Profile in Healthy Non-Obese Male Wistar Rats

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Obesity a ects one-third of the general population [1]. In 2014, the World Health Organization estimated that there were more than 1.9 billion adult overweight people of whom more than 600 million were obese [2]. More than 115 million people are estimated to have obesity-associated diseases such as cardiovascular disease, stroke, diabetes, dyslipidaemia, obstructive sleep apnea, metabolic syndrome, and breast, colon, and liver cancers [3].

Changes in diet and exercise are the mains preventive and management approaches for obesity. However, the majority of obese patients are unable to accomplish or sustain intentional weight reduction by diet and exercise alone [4]. Over the last two decades, human and animal studies have shown that timing of meal intake is as important as the composition of the diet and caloric quantity to prevent obesity and its complications [5-8]. Mealtime and cultural eating habits, the quantity, and type of foods ingested can adversely a ect health status and increase the likelihood of developing obesity and related complications. It has been suggested that time-restricted food intake might be a successful intervention to prevent and manage obesity, metabolic syndrome, and its complications [9-11].

Behavioral weight loss approaches are e ective at helping individuals reduce weight by 5-10% of their initial body weight [12,13], but a primary public health goal remains prevention of obesity, along with identifying behavioral strategies to optimize weight loss and maintenance. Of the many factors contributing to the obesity epidemic, the timing of food consumption has become the subject of much recent attention for its signi cant contribution to body weight regulation [14,15]. Notably, food timing is a potentially modi able behavioral target, and as such, deserves critical examination for its possible role in achieving weight loss or weight maintenance.

Intermittent fasting (IF) is an increasingly popular dietary approach used for weight loss and overall health. While there is an increasing body of evidence demonstrating bene cial e ects of IF on blood lipids and other health outcomes in the overweight and obese, limited data are available about the e ect of IF in healthy non- obese animals or humans. is study therefore aimed at investigating the e ect of 4 hour time-restricted feeding on body weight, leptin concentration and lipid pro le in healthy non-obese male Wistar rats.

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– 8 am -12 pm; 12 pm - 4 pm; 8 pm -12 am for a period of 4 weeks. is diet strategy resembles taking only breakfast, lunch or dinner once a day for a period of 4 weeks.

E

Twenty four rats divided into four groups (n=6) were used. Group I animals were placed on a 4 hour per day TRF between 8 am-12 pm. Group II rats were also placed on a 4 hour per day TRF between 12 pm - 4 pm. Group III rats also placed on a 4 hour per day TRF between 8 pm -12 am while Group IV rats had access food and water ad libitum. e study lasted for a period of 4 weeks.

M

Body weight of rats was measured weekly using a weighing balance. e percentage (%) weight gain was calculated as: (body weight on speci c week (g) − initial body weight)/initial body weight ×100. Food intake was measured once a week over 24 h based on the weight of le over feed out of 160 g given.

S

At the end of treatment period, the rats were anesthetized with sodium pentobarbital. Blood was collected by cardiac puncture into heparinized bottle and was centrifuged at 3000 g for 5 mins. Plasma was stored frozen until needed for biochemical assay.

B

Rats were fasted for 12 h before blood glucose measurement. Food was removed from the food dispenser and bedding of the cages was changed to avoid coprophagy. Blood from the tail vein was measured for glucose using the OneTouch Basic glucose monitor (Lifescan) and reported as mg/dl. Blood glucose level was measured during the study and prior to sacri ce. Fasting plasma levels of total cholesterol (TC) and triglyceride (TG) were measured by standardized enzymatic colorimetric methods using assay kit obtained from Fortress Diagnostics Ltd. (Antrim, UK). High-density lipoprotein-cholesterol (HDL-C) was measured by enzymatic clearance assay (Daiichi Pure Chemicals Co., Ltd., Tokyo, Japan) whereas low-density lipoprotein-cholesterol (LDL-C) was estimated using modi ed Friedewald's formula. TC/HDL-C and TG/HDL-C ratios were estimated as marker of atherogenic lipid indices. Plasma leptin was determined using enzyme-linked immunoabsorbent assay (ELISA) kits following manufacturer's instruction (leptin: RayBio® Rat Leptin ELISA Kit, Cat # ELR-Leptin-001, Norcross, GA, USA).

D

All data were expressed as means ± SEM. Statistical group analysis was performed with SPSS statistical so ware (version 21). One-way analysis of variance (ANOVA) was used to compare the mean values of variables among the groups. Bonferroni's posthoc test was used to identify the signi cance of pair wise comparisons of mean values among the groups. Statistically signi cant di erences were accepted at $p<0.05$.

R

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e body weight of 8 pm -12 am and ad libitum groups signi cantly increased compared with the 8 am -12 pm and 12 pm-4 pm groups (Figures 1 and 2).

B

e fasting blood glucose levels of the normal and the time-restricted fed rats were shown in Figure 3. Fasting glycemia in the 12 pm - 4 pm fed rats increased signi cantly when compared with the other three groups.

C

Figure 4 depicts the lipid pro le of the normal and the time-restricted fed rats. ere were signi cant increases ($p<0.05$) in the total cholesterol (TC), triglyceride (TG) and very low density lipoprotein cholesterol (VLDL-C)levels of group fed ad libitum when compared with the 8 am -12 pm and 12 pm - 4 pm groups. However, there was

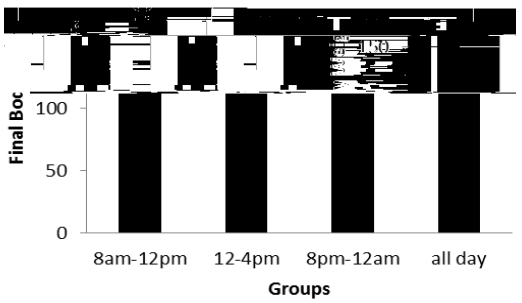


Figure 1: Physiological parameter body weight.

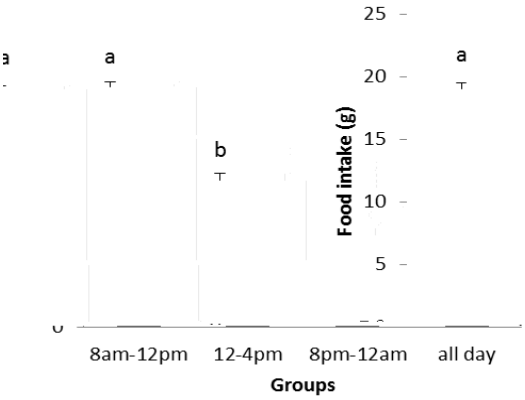


Figure 2: Physiological parameter food intake.

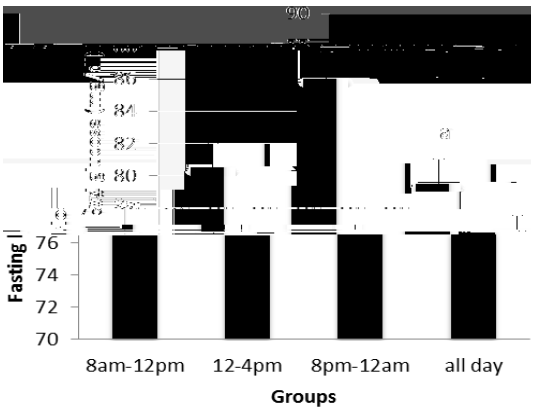
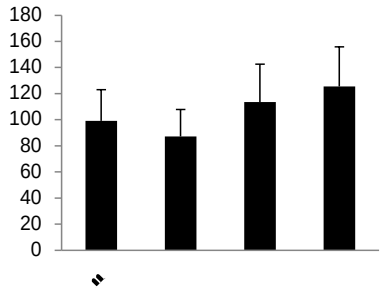


Figure 3: The fasting blood glucose levels of the normal and the time-restricted fed rats.


180
160
140
120
100
80
60
40
20
0

the development of dyslipidemia [22]. Results from this work showed altered circulating plasma lipid concentrations i.e dyslipidemia. ere were signi cant increases in TC, TG, LDL-C and VDLC-C concentrations with a signi cant decrease in HDL-C concentration in the 8.00 pm - 12 am and ad libitum rats compared to other regimes of TRF.

Several epidemiological studies have established that dyslipidemia is a major cause of cardiovascular disease [23,24]. Altered circulating lipid concentrations are recognized as risk factors for cardiovascular diseases (CVDs) [25]. CVDs are the leading cause of global premature mortality and disability [26]. It has also been shown that an increased level of TC (hypercholesterolemia), particularly LDL-C promotes the atherosclerosis process, leading to the deposition of cholesterol and fatty acids in the artery wall, whilst HDL-C is usually considered to be protective and returns cholesterol to the liver [27,28]. Epidemiological studies including that of the American Heart Association have also shown that elevated TG levels correlate with elevated CV risk, thus elevated TG levels are an important marker of CV risk [29,30].

is diet strategy of 4 weeks of 4-h TRF(between the hours of 8 am – 12 pm and 12 pm -4 pm) suggests cardio-protective e ects in non-obese rats, by lowering total cholesterol, triglycerides, LDL and VLDL while increasing HDL cholesterol concentrations. ese changes in lipid risk factors are in line with what has been reported for obese alternate day fasting (ADF) subjects [31]. Also, In two ADF studies, triacylglycerols decreased by 15% a er 8 weeks of treatment in obese men and women [32]. us, TRF may improve plasma lipids in non-obese subjects as it does in obese subjects. Our results were also con rmed by previous researches suggesting a positive e ect of TRF (between the hours of 8 am -12 pm, 12 pm - 4 pm) on blood lipid pro les [33-35].

Additional vascular bene t including decrease in circulating leptin was also noted in non-obese rats in our diet strategies of TRF compared to the group fed ad libitum. e group fed ad libitum has an outrageous elevated signi cant leptin level compared to the TRF groups Leptin is a 16 kDa hormone mainly secreted by adipocytes and is involved in the control of food intake via its action on the hypothalamus, leading to the suppression of appetite [36]. erefore, leptin is an “anorexigenic” hormone. However, obesity is characterized by hyperleptinemia due to the development of leptin resistance [37]. Scarpace and Zhang (2007) also reported a positive correlation between elevated leptin level and the development of leptin resistance and obesity [38]. Apart from obesity, hyperleptinemia has been also associated with hypertension and insulin resistance [39,40]. e peripheral actions of leptin include stimulation of in ammatory reaction, oxidative stress, atherogenesis and thrombosis, thus promoting endothelial dysfunction, arterial sti ness, development and vulnerability of atherosclerotic plaques [41,42]. Higher leptin levels have also been considered to be the cause of infertility [43].

Results from this study also suggest that of all the TRF groups, the 8 am -12 pm, which is a representation of breakfast consumption was the most bene cial since it prevents dyslipidemia, increase in body weight, blood glucose and leptin concentrations. Regular breakfast consumption has been reported to improve several metabolic parameters, mostly associated with cardiovascular risk, reducing circulating LDL cholesterol levels, LDL oxidation and lowers blood triglycerol concentrations [44-46]. is also brings to mind the quote of the nutritionist Adelle Davis (in the 1960s), which says: “Eat breakfast like a king, lunch like a prince and dinner like a pauper” [47].

In conclusion, 4-h time restricted feeding for a period of 4 weeks has bene cial e ects on body weight, blood glucose, lipid pro le and leptin concentration in healthy non-obese male Wistar rats.

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