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The Ameliorating Effects Of Ginger And Turmeric On The Body Weights And Heart Body Weight Ratio Following Streptozotocin Induced Diabetes Mellitus In Albino Rats (*Rattus Norvegicus*)

Caroline C. Sigei[1], Kweri J Kariuki[1], Thuo Reuben[1], Dominic Marera[2]
1 (College of Health Science, Jomo Kenyatta University of Agriculture and Technology, Kenya))
2(College of Health science), Maseno University, Kenya)

Abstract:
Background*: Diabetes mellitus is a metabolic disease characterized by prolong high blood sugars due to impaired insulin secretion, resistance or both[1]. The increase in body weight, otherwise known as obesity has been associated with diabetes mellitus[2]. The global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045)[3]. Cardiovascular disease is the leading cause of mortality among patients with diabetes mellitus which could be due to cardiovascular risk factors such as obesity, high heart body weight ratio among others[4]. The use of Ginger and turmeric has been shown to improve the heart functions in diabetic patients with cardiovascular disease through various mechanisms such as reduction in total cholesterol and serum triglycerol hence reducing body weight, increasing insulin and leptin levels leading to reduced blood sugar levels[5]. However, there is paucity of data on whether these two herbaceous medicine have better outcome when used as monotherapy or as a combined therapy.*
Broad Objective*: To evaluate ameliorating effects of ginger and turmeric on the blood glucose levels, body weights and heart body weight ratio following streptozotocin induced diabetes in Albino Rats.*
Materials and methods*: True experimental laboratory based study design was used in this study. The study was carried out in the University of Nairobi animal house for 16 weeks, Daily body weights and weekly blood sugars were measured. A sample size of 30 male adult albino rats from a pure colony were used. The animals were randomly assigned to either 3 rats control or 27 rats experimental. The control (Group I) received normal diet. In the experimental group the induction of diabetes was done using high fatty diet for six weeks then single dose of streptozotocin (STZ) 65mg/kg administered through intraperitoneal injection after which the blood glucose was tested after 48 hours using blood glucose meter. Rats with glucose above 16.7 mmol/l was used to confirm diabetes and they were randomly selected into nine treatment groups with three rats each (Group II-X). In order to compare the effects of ginger and turmeric, the experimental group was randomly assigned to various subgroups that received different interventions of ginger and turmeric as monotherapy and combined, early treatment from 7-16 weeks and late treatment 11-16 weeks. All animals were humanly sacrificed end of week 16 using concentrated carbon dioxide. Their chest walls were resected and the hearts were obtained, weighed and recorded for morphometric analysis.*
Data entry and analysis: *Data was analyzed using SPSS for windows version 25 and statistically tested using one-way ANOVA.*
Results*: The findings on the mean body weights of the diabetic group showed significant decrease in mean body weight and increase in heart body weight ratio while the mean body weights among ginger turmeric treatment groups was decreased and the heart body weight ratio was low compared with that of the control group. The effects of ginger and turmeric on the body weights and the heart body weight ratio were significantly different between the combined ginger turmeric treated groups particularly when administered early compared to when administered later and as a monotherapy.*
Conclusion*: The use of combined ginger and turmeric maintain average body weight and lower the heart body weight ratio in streptozotocin induced diabetes mellitus albino rats .*
Key Words*: Ginger; Turmeric; Body weight; Heart body weight ratio; Diabetes mellitus; Albino rats.*

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I. Introduction

Diabetes, a metabolic disease that occur due to defect in insulin secretion, function or both, characterized by abnormal rise in blood sugars and over time leads to damage of organs such as the heart, blood vessels, kidneys, nerves among others[6]. Diabetes mellitus is a major health problem that affected approximately 462 million people globally in 2017 and it is projected to increase to 7079/100,000 individuals by the year 2030 and it is the ninth leading cause of over 1 million deaths per 100,000 individuals[7]. There is a close relationship between diabetes, increased body weight and cardiovascular disease, the latter being the leading cause of morbidity and mortality[8]. Proper management of the diabetes mellitus and the associated cardiovascular risk factors such as obesity is important in reducing the increasing prevalence of diabetes and the cardiovascular disease[9]. Ginger and turmeric are herbaceous medicine which have been shown to alleviate such cardiovascular risks among diabetics. However, there is paucity of data on their effects on the body weight and heart body weight ratio as cardiovascular risk factors in diabetes and whether the outcome is better when the two are used as combined therapy rather than as a monotherapy.

Ginger is one of the most widely consumed spices globally. It is an underground rhizome used as an herbal medicine with anti-inflammatory, anti-oxidative characteristics among others and belongs to plant *Zingiber officinale* of Zingiberaceae family[10]. Ginger gingerols, shogaols, and volatile oils which are beneficial to diabetic patients[11]. Ginger, in a study has been shown to have anti-diabetic activity in that pretreatment using ginger inhibited the induced hyperglycemia and hypoinsulinemia[12]. Further, ginger has been shown to be protect myocardial damage through suppression on of hyperlidemia and cardiac biomarkers[13].

Turmeric, also known as (*Curcuma longa*) with an active component called diferuloylmethane[14].It is a yellow pigment that is used worldwide as food additive, cosmetics, dyes, and medicines[15]. Turmeric have been shown to be protective against diseases which are autoimmune, pulmonary problems as well as cancer[16]. It lowers the lipids and protects the heart[17]. Turmeric has been shown to reduce oxidative stress as well[18].

The cardiovascular risk factors in diabetes include obesity, hypertension, dyslipidemia, diabetic cardiomyopathy, cardiovascular autonomic neuropathy, myocardial infarction, poor glycemic control among others. Obesity is common in diabetes mellitus and it is attributed to cardiovascular disease in diabetes due to overexpression of cytokines and lipid accumulation that cause inflammation and dysfunction of the endothelium[19,20]. Loss of weight has been shown to improve the cardiovascular risk profile in patients with diabetes[21]. The fluctuation in body weight was associated with higher mortality and a higher rate of cardiovascular events, independent of traditional cardiovascular risk factors in patients with diabetes mellitus[22].

Diabetes mellitus is associated with high blood glucose levels and this is associated with worse risk to the cardiovascular structures if poorly controlled. Well monitored and controlled glucose levels using drugs, moderate weight loss and lifestyle modification improves cardiovascular outcomes[23]. The hypertrophy of the heart is common in diabetes mellitus and this consequently leads to increased heart weight and heart failure which is the leading cause of death in patients with diabetes[24].

II. Material and Methods

Study site/Location: All experiments that included breeding, handling, weighing, drug administration and measurements of all the parameters was done at the animal Facility situated in the University of Nairobi.

Study Design:A laboratory based experimental study design was adopted

Acquisition and feeding of the albino rats: The albino rats were purchased from the animal facility in the University of Nairobi. They were fed on a standard diet as determined by American institute of nutrition (2011) that included rodent pellets and water *adlibitum.* They were kept in spacious polycarbonate plastic cages in the animal house as determined by[25].

Sample size calculation: In calculating the sample size, resource equation was applied to get the 30 albino rats used for the study[26]. The formula states that the measured value 'E' which is the degree of freedom of analysis of variance (ANOVA) based on a decided sample size value ('E') should lie between 10 and 20 animals according to this equation. Therefore, a value less than 10 necessitates adding more animals which increases the chance of getting significant results while a value more than 20 has been shown to increase the cost of the study without increasing the significance of the results. Therefore, total number of groups=10 while the total number of animal sis 30. E=Total number of Animals-Total number of groups. E is therefore is 30-10 which is 20

Grouping of animals: A total of 30 nulliparous albino rat dams of the species Rattus norvegicus weighing between 200-250g were derived from a pure colony were used as the animal experimental model in this study. The 30 dams were calculated using the resource equation method (E=TA-TG) was divided into 10 groups; The control (Group I) received normal diet. Group II- equivalent ml of water as for the other interventions; Group III-

ginger 200mg/kg bwt from week 7-16 , Group IV- ginger 200mg/kg bwt from week 7-16, Group V- turmeric (150mg/kg bwt) from week7-16, Group VI will receive turmeric 150mg/kg bwt from week 11-16, Group VII- combined ginger (200mg/kg bwt) and turmeric (150mg/kg bwt) from week 7-16, Group VIII- combined ginger(200mg/kg bwt) and turmeric(150mg/kg bwt) from week 11-16, Group IX -metformin 50mg/kg from 7-16 weeks, Group X- metformin, ginger and turmeric combined from week 11-16

Determination of drug doses: A simple guide for conversion of human to animal dosages was used[27].The correction factor (Km) is estimated by dividing the average body weight (kg) of species to its body surface area (m2). For example, the average human body weight is 60 kg, and the body surface area is 1.62 m2. Therefore, the Km factor for human is calculated by dividing 60 by 1.62, which is 37. The Km factor values of a rat is used to estimate the HED as: HED mg / kg = Rat dose mg / kg Animal K /Human K Eq. As the Km factor for each species is constant, the Km ratio is used to simplify calculations. Hence, Equation is modified as: HED mg / kg = Animal dose mg / kg K ratio Eq. The Km ratio values are already provided and are obtained by dividing human Km factor by animal Km factor or vice versa. Ginger and Turmeric administration was done using an oral gavage needle gauge 16.

Administration of drugs: In the experimental group the induction of diabetes was done using high fatty diet for six weeks then single dose of streptozotocin (STZ) 65mg/kg administered through intraperitoneal injection after which the blood glucose was tested after 48 hours using blood glucose meter. Rats with blood glucose below 16.7mmol/l was given streptozotocin the second time and those with blood glucose above 16.7 mmol/l
All animals in the early treatment groups received ginger and turmeric from week 7 to week 16 while the animals in late treatment groups received from week 10 to 16.

Weighing of the animals: During the experimental period, body weights were measured and recorded daily using a digital scale.

Statistical analysis: The study examined the effects of Ginger and turmeric on the body weight trends and the heart weight in diabetic albino rats.
The data was analyzed using SPSS version 25 and was expressed as mean ± standard error (SEM). The study compared the body weight trends, the heart weight outcomes and heart body weight ratio when the two medicines were administered as single drug and as a combination.

Ethical Approval: All procedures for animal handling, feeding, humane sacrificing and harvesting of organs were performed as per laid down protocols, with approval from Animal Ethics Committee University of Nairobi REF: FVM BAUEC/2021/341**)**

III. Results

The effects of ginger and turmeric on the mean body weight trends

The findings on the mean body weight trends among ginger and turmeric treatment groups were average and constant from week 6-16 that is during the treatment period. However, the weight was lower compared to that of the control. There was consistent decrease (lowest) in the mean body weight trends of the diabetic group compared to that of the control (highest) as shown in figure 1 below.

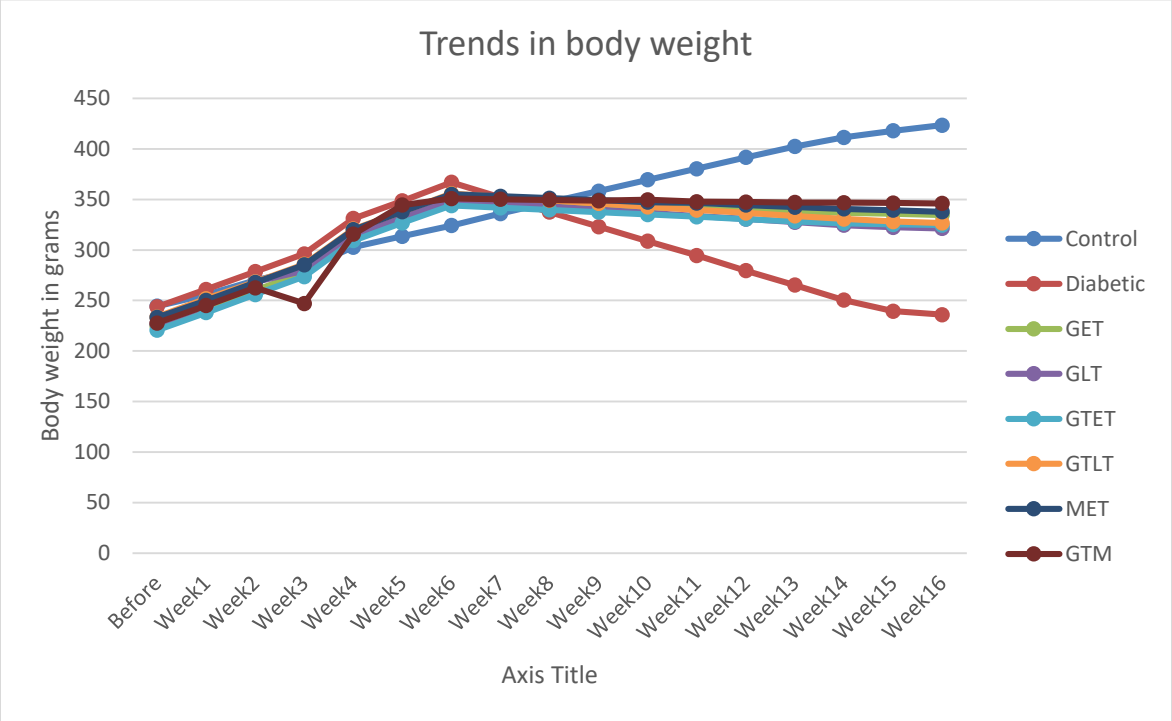

Figure no 1: Shows the mean body weight trends from day 0 to week 16 in ginger turmeric treatment groups, diabetic group and that of the control in albino rats.

The effects of ginger and turmeric on the mean terminal body weight

The mean body weight at sixteen weeks was lowest and significantly different in the non-treated diabetic group (236 ± 2.65) compared to the mean weights of the ginger turmeric treated groups and that of the control (423.53 ± 2.33). Significance difference was also noted between combined ginger and turmeric when administered early (350.13 ± 4.66) when compared to when administered late (335.27 ± 6.06). There was no significance difference in the mean body weights of the ginger and turmeric treatment groups particularly when administered as a monotherapy as shown in table 1 below.

The effects of ginger and turmeric on the mean heart body weight ratio

The results showed statistical significance difference in the mean heart body weight ratio (2.91 ± 0.43) when ginger turmeric was administered early as a combined therapy when compared to that of the control (2.83 ± 0.15^{a}) and the other ginger turmeric treatment groups that received either ginger or turmeric as a monotherapy. The mean heart body weight ratio was statistically significantly high in the non-treated diabetic group (3.81 ± 0.79) compared to that of the control (2.83 ± 0.15^{a}). Statistical significant difference was also noted between all ginger and turmeric treatment groups from that of the non-treated diabetic group as shown in table 1 below.

Table no 1: Shows the comparative means of the body weights and hearts weights in Ginger, Turmeric and combined ginger turmeric in early and late treatment against diabetic (D) and the control.

Study groups	**Period of treatment**	**Mean end body weight (g) + SEM**	**Mean heart weights (mg) + SEM**	**Mean heart body weight ratio(g/kg)**
Control	-	423.53 ± 2.33^{a}	1154.83 ± 4.77^{a}	2.83 ± 0.15^{a}
GTM	Early	$346.00 \pm 1.46^{b*}$	1053.93 ± 1.95b	3.15 ± 0.34^{b}
GET	Early	338.53 ± 3.55c	1052.30 ± 3.61b	3.01 ± 0.51^{b}
MET	Early	337.47 ± 2.44c	1046.01 ± 3.09^{b}	3.10 ± 0.27^{b}
GTET	Early	$350.13 \pm 4.66^{b*}$	1020.73 ± 2.52c*	2.91 ± 0.43^{a}
GTLT	Late	335.27 ± 6.06c	1052.53 ± 2.89b	3.05 ± 0.38^{b}
TLT	Late	326.77 ± 12.45c	1005.83 ± 3.70c*	3.11 ± 0.41^{b}

TET	Early	324.63 ± 5.50c	1015.63 ± 1.94^{c*}	3.03±0.36^{b}
GLT	Late	321.27 ± 5.95c	1025.07 ± 3.02^{c}	3.18±0.40^{b}
D		236.11 ± 2.65^{d*}	893.90 ± 5.13^{d*}	3.81±0.79^{c*}

*The means, followed by the same letter in a column are not statistically different at (p 0.05) using one-way ANOVA with Tukey test on post-hoc t-tests. *iindicates significance (p < .05)*

IV. Discussion

Diabetes mellitus (DM) is a metabolic disease, involving inappropriately elevated blood glucose levels[28]. Diabetes has been associated with severe weight loss with chances of complications[29]. The results of the present study showed constant and average weight trends among ginger and turmeric treated groups indicating minimal weight gain when compared to that of the control as well as minimal weight loss when compared to that of the non-treated diabetes in streptozotocin induced diabetes mellitus. (Figure 1).

The moderate body weight loss observed among the diabetic treated rats administered with turmeric could be primarily because of its effectiveness in reducing glycemia and hyperlipidemia by increasing the rate of glucose catabolism and biosynthesis of fat and protein in rodent models[30]. Subjects with weight gain ≥ 10% had a significantly higher risk of stroke and the group with weight loss ≥ − 10% had the highest HR for all-cause mortality[31]. This explains the importance of maintaining a constant average body weight among patients with diabetes mellitus.

The results of this study showed lower heart body weight ratio among the ginger turmeric treatment groups compared to the non-treated diabetic group. Though the heart body weight ratio among all the treatment groups were higher than that of the control, the outcome showed no statistical difference between the group that received early treatment of combined ginger and turmeric when compared to that of the control. The study done in Iran showed that weight gain > 5% was associated with better cardiovascular/ coronary disease outcomes among participants with T2DM [32]. Inhibition of high blood glucose levels and increase body weight without affecting the heart/body weight ratio by use of resveratrol was shown to be protective against cardiovascular complications such as myocardial infarction related to diabetes mellitus[33].

V. Conclusion

Combined ginger and turmeric ameliorated diabetes mellitus, maintain average and constant body weight, alleviates heart body weight ratio in streptozotocin-induced diabetes mellitus albino rats. Therefore, ginger and turmeric could serve as a potential natural and safe remedy for the management of diabetes mellitus and/or delay in diabetic cardiovascular complications.

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