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EFFECTS OF 25GMS/KG, 50GMS/KG AND 75GMS/KG OF BODY WEIGHTS OF GARCINIA CAMBOGIA PLANTS ON BLOOD GLUCOSE LEVELS OF DIABETIC RATS----AN ANIMAL MODEL STUDY.

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ABSTRACT

BACKGROUND: Type 2 Diabetes Mellitus (T2DM) affects an estimated 462 million people worldwide, accounting for roughly 6.28% of the world's population. **OBJECTIVE:** The study is aimed to determine the potential effects of alternative medicine in the management of T2DM as many medicinal plants and its product have traditionally been used since ancient time and one such medicine plant is Garnicia Cambogia that belongs to the family Clusiaceae widely known as Malabar Tamarind. Hence, the present study is aimed to determine the effects of ancient medicine approach by using Garnicia Cambogia plant extract in the management of T2DM in animal model. **METHODOLOGY:** A total number of n=100 Wistar rats were divided into five groups. Rats were procured from the Basic Medical Sciences Institute's Open Market/Animal House at JPMC Karachi. While housing and handling the rats, the researchers scrupulously adhered to the rules established in the NIH Guide for the Care and Use of Laboratory Animals**. RESULTS:** The negligible P-value (P = 0.57) supports this conclusion, demonstrating that there was no significant variation in body weight between the rat groups. The fact that the rat groups had equal baseline body weights eliminates any study bias and allows for a more accurate comparison and interpretation of the experimental data**. CONCLUSION:** The study suggests that Garcinia Cambogia plant extract has favourable benefits on blood glucose levels and glycemic control in an animal model of type 2 diabetes, especially at higher dosages.

KEY WORDS: Garnicia Cambogia, T2DM, Alternative Medicine, Medicinal Plants

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) affects an estimated 462 million people worldwide, accounting for roughly 6.28% of the world's population. Because of its high frequency, the disease accounted for approximately 1 million fatalities in 2017, making it the tenth greatest cause of death. Diabetes-related fatalities are on the rise, particularly when contrasted to their ranking as the eighteenth largest cause of death in 1990[1]. Several

locations, notably Pacific Ocean island nations, have the greatest frequency of type 2 diabetes, with countries such as Fiji, Mauritius, American Samoa, and Kiribati seeing alarming rates[1-2]. Over the last two decades, the prevalence of type 2 diabetes has risen in Southeast Asian nations such as Indonesia, Malaysia, Thailand, and Vietnam. However, large nations such as China, India, and the United States rank first in terms of overall number of people affected by type 2 diabetes[3]. Type 2 diabetes affects an estimated 88.5 million people in China, 65.9 million in India, and 28.9 million in the United States. These figures highlight the worldwide aspect of the diabetes epidemic, which affects both small countries with high prevalence rates and large countries with enormous populations[4]. To address the disease's burden and its accompanying problems, efforts to prevent and treat type 2 diabetes must be prioritized at both the regional and national levels. While males have a slightly greater prevalence of type 2 diabetes (6219 cases per 100,000) than females (5898 cases per 100,000), this difference is within the margin of uncertainty. Interestingly, males seem to have a little younger age of onset for new diseases[5]. As predicted, the prevalence of type 2 diabetes rises with age, with the 55-59 age group having the highest incidence. Unexpectedly, the age distribution of type 2 diabetes patients did not change much from 1990 to 2017, showing that the disease's burden has stayed largely consistent over time. These findings emphasize the need of maintaining a focus on diabetes prevention and treatment techniques for people of all ages and genders[6]. Management of T2DM ranges from life style modification to pharmacotherapy based on its pathophysiology, however according to its mode of action Diabetes medications are classified into many classes[7]. Biguanides (e.g., metformin) and thiazolidinediones are insulin sensitizers that increase insulin sensitivity and reduce insulin resistance[8]. Insulin sensitizers, such as sulfonylureas and meglitinides, promote pancreatic insulin secretion, boosting glucose absorption. Acarbose and other alpha-glucosidase inhibitors slow carbohydrate absorption in the gut[9]. GLP-1 receptor agonists (GLP-1 receptor agonists) and dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors) are incretin-based medicines that modulate insulin secretion and glucagon release. Sodium-glucose cotransporter 2 (SGLT2) inhibitors, such as canagliflozin and dapagliflozin, increase urine glucose excretion, lowering blood glucose levels[10]. Lipase inhibitors, such as orlistat, prevent the absorption of dietary fat. Amylin agonists, which are hormone mimics, regulate blood sugar levels by decreasing glucagon release and inducing satiety[11-12]. Finally, insulin, which can be supplied through injection or pump, is utilized when other treatments are inadequate. Individual patient variables, disease progression, and treatment objectives all influence the choice of diabetes medications. Although various form pharmacological therapy management approaches for T2DM are available but the cost incurred in its management is enormous and according to evidences available in literature T2DM cost Sub-Saharan Africa USD 19.45 billion in 2015 alone, accounting for 1.2% of the region's gross domestic product (GDP)[13-14]. Direct medical expenditures accounted for more than 55% of this financial burden, highlighting the significant impact on healthcare systems. Furthermore, in many countries, out-of-pocket spending for diabetes care likely exceeded 50% of overall health expenditure[15]. It is therefore this study is aimed to determine the potential effects of alternative medicine in the management of T2DM as many medicinal plants and its product have traditionally been used since ancient time and one such medicine plant is Garnicia Cambogia that belongs to the family Clusiaceae widely known as Malabar Tamarind. Hence, the present study is aimed to determine the effects of ancient medicine approach by using Garnicia Cambogia plant extract in the management of T2DM in animal model.

Methodology

Study Design

Animal Experimental Study.

Study Setting

The research was conducted at Animal House with the assistance of the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, JPMC Karachi.

Animal Housing

Albino Wistar rats were procured from the Basic Medical Sciences Institute's Open Market/Animal House at JPMC Karachi. While housing and handling the rats, the researchers scrupulously adhered to the rules established in the NIH Guide for the Care and Use of Laboratory Animals. The rats were kept in stainless steel cages with sawdust bedding, stainless steel feed containers, and plastic drinks with stainless nozzles. The rats were kept in a clean and well-ventilated habitat thanks to the housing environment. They could eat lab chow and

drink tap water whenever they wanted. To imitate a natural day-night cycle, the light and dark cycles were kept at 12-hour intervals. The Animal House of the Basic Medical Sciences Institute, JPMC Karachi, performed all animal procedures in line with an established animal protocol. To discriminate between the several rat groups being investigated, the cages of rats in the control and experiment groups were properly labelled.

Experimental Protocol

A total number of n=100 Wistar rats were divided into five groups n=10 rats in each group. The groupings of rats were as follow:

Control Group

Group A (n=20): Control rats are given 0.9% normal saline as a placebo.

Groups of Experimenters

Group B (n=20): Diabetes mellitus induced by administering Alloxan 120 mg/kg body weights intraperitoneally

Group C (n=20) Diabetic rats + GcE (25 g/kg bwt) daily for 8 weeks,

Group D (n=20) Diabetic rats + GcE (50 g/kg bwt) daily for 8 weeks,

Group E (n=20): Diabetic rats + GcE (75 g/kg bwt) daily for 8 weeks,

Garcinia Cambogia content was equivalent to 1000, 2000, and 3000 mg/kg of GcE-HCA levels. Wilshire Pharmaceuticals Pakistan provided the Garcinia Cambogia extracts (G-Lite) containing (-)-HCA. The product's batch number, production date, and expiry date were meticulously confirmed.

Outcome Measures

Blood Glucose levels at Fasting and Random

Blood glucose levels were measured biochemically using the most recent Hexokinase (H-kinase) technique and analysed on a cutting-edge 'Hitachi-Roche' Cobas Chemistry Analyzer produced by Roche, USA. This cutting-edge equipment ensured that blood glucose levels were accurately and consistently measured. The evaluations were performed at two points: baseline and week 8, allowing for a thorough investigation of any changes in glucose levels throughout the course of the trial. The research team gained useful insights into the dynamics of blood glucose and its possible changes over the study period by using cutting-edge technology and accurate analytical methodologies[16].

Glycated Hemoglobin Concentration (HbA1C)

The TTAB (tetra-decyl-tri-methyl-ammonium bromide) technique was used to assess the amounts of glycated haemoglobin (HbA1c) in the samples. The samples were analyzed using an advanced Chemistry Analyzer, especially the Hitachi Roche Diagnostics Chemistry Analyzer 902, which was made in the United States. The TTAB technique, as previously mentioned, was used to accurately quantify HbA1c levels. A turbid-metric inhibition immuno-assay (TINIA) approach was utilized to evaluate hemolyzed or whole blood samples. The "IFCC" (International Federation of Clinical Chemistry and Laboratory Medicine) approach was used to standardize this procedure, assuring trustworthy and consistent findings. HbA1c levels were assessed at both the baseline and week 8 intervals, providing for a thorough assessment of any changes in HbA1c levels during the given time frame. The researchers gathered accurate and useful information regarding HbA1c levels throughout the trial by using cutting-edge equipment and standardized methodologies[17].

Results

Baseline Characteristics

The baseline body weight of both control and experimental rats was discovered to be the same in all groups. The negligible P-value (P = 0.57) supports this conclusion, demonstrating that there was no significant variation in body weight between the rat groups. The fact that the rat groups had equal baseline body weights eliminates any study bias and allows for a more accurate comparison and interpretation of the experimental data (table 1).

Table 1 Comparative analysis of Baseline Characteristics of rats in term of Weights measured in grams

Variables	Average weights in grams± SD	F-Value	Level of Significance
Group A	177.05±11.73	0.726	0.57
Group B	175.05±14.23		
Group C	174.35±11.21		
Group D	177.70±5.77		
Group E	171.80±16.06		

Effect of experimental protocol on body weight

The negative control group, A, had a substantial rise in post-experiment body weight (g), with a mean weight of 319.35 ± 33.05 grams (Table-2). After an 8-week period, the positive control group, B, likewise increased in body weight from 175.05 grams to 204.10 grams. The low P-value (0.001) suggests a significant difference in body weight between the control and experimental rat groups, emphasizing the importance of experimental conditions on weight changes. Table-2 also shows the post-experimental body weight of the experimental rat groups C, D, and E, revealing more about the impact of the treatments on their different body weight outcomes.

Table 2 Comparative analysis of Weights measured in grams after eight week of experiment

Variables	Average weights in grams± SD	F-Value	Level of Significance
Group A	319.35±33.05	28.57	0.001
Group B	204.1±22.25		
Group C	292.05±43.15		
Group D	294±50.16		
Group E	304.95±35.15		

Effects of intervention on FBS, RBS and HbA1C levels

The fasting blood sugar levels in the negative control group A was 78.1±11.3 mg/dl, while in group B the values were 323.923.9 mg/dl. However, in the GcE-treated experimental groups C, D, and E, FBS levels reduced to 256.123.7 mg/dl, 252.031.2 mg/dl, and 219.521.4 mg/dl, respectively. The p-value of 0.001 found indicates that the drop in random blood sugar levels in the GcE-treated experimental rats that was statistically significant. In addition to that on RBS levels in the negative control group A had starting levels of 126.15 ± 7.3 mg/dl, but the positive control group B had levels that were substantially higher at 447.0 ± 30.0 mg/dl. However, as compared to the positive control group B, the experimental groups C, D, and E that received GcE therapy saw significant reductions in blood sugar levels. Group C obtained 321.8 ± 9.19 mg/dl, group D achieved 304.0 ± 7.05 mg/dl, and group E had the greatest decrease, with levels decreasing to 242.1 ± 37.4 mg/dl. The calculated p-value of 0.001 suggested a statistically significant drop in blood sugar levels in the experimental rats following the 8-week GcE therapy. Finally the effects on GcE treatment on glycated hemoglobin concentration had also shown significant findings the values were significantly lower in experimental groups C, D, and E. Group C had a fall of 8.27 ± 0.46, group D had a decline of 7.37 ± 0.48, and group E had the greatest decrease, with levels decreasing to 6. ±.41. These figures were compared to the negative control group A where the values HbA1C were 3.85±0.32 and the positive control group B where the values were 8.7 ± 0.58. The statistical analysis demonstrated that GcE efficiently modifies glycemic control in the treated groups (F-value = 356.1, P < 0.0001). These findings emphasize GcE plant potential as a beneficial impact in blood sugar management (table 3).

Table 3 Effects of Garcinia Cambogia plants on blood glucose levels of Alloxan induced DM rats

Variables	FBS	F value	p-value	RBS	F value	p-value	HbA1C	F value	p-value
Group A	78.1± 11.31	311.1	0.0001	126.17± 7.3	555.9	0.0001	3.85±0.32	356.1	0.0001
Group B	323.95±23.11			447.05± 30.01			8.7±0.58		
Group C	256.15±23.73			321.8± 9.19			8.27±0.46		
Group D	252.05±31.22			304± 7.05			7.37±0.48		
Group E	219.55±21.44			242.15± 37.43			6.38±0.41		

DISCUSSION

The purpose of this animal model study was to see how different dosages of Garcinia Cambogia (GC) plants affected blood glucose levels in diabetic rats. The research looked at the efficacy of 3 dosages: 25gm/kg, 50gm/kg, and 75gm/kg of body weight.

Findings demonstrated that those in the group obtaining the maximal dose of 75gms/kg of GC plant saw a significant decrease in the amount of glucose in their blood as contrasted with the control group that received placebo A. According to these findings, a higher dose of GC plant extract seemed beneficial in lowering glucose levels in the blood in diabetic rats. In addition, the 75gm/kg dosage of GC plant extract reduced the levels of glucose in the blood with greater effectiveness than the alloxan-induced group B, which served as a diabetic control. It demonstrates the fact GC extracts of plants can shield rats with diabetes from alloxan's hyperglycemic consequences. Unexpectedly, the lesser doses of 25gm/kg & 50gm/kg of GC extracts from plants have similarly significantly significantly influenced the level of glucose in the blood when contrasted with the control groups; nevertheless, larger quantity had efficacy over lower dosage. That demonstrates a dose-dependent relationship, with the greater dose of 75 g/kg being more effective in controlling the levels of glucose in the blood in this kind of animal species. Overall, our data show that GC plant extract has a dose-dependent impact on blood glucose levels in diabetic rats. The study focuses on the possibility of greater dosages of GC plant extract, namely 75gms/kg, as a possible therapeutic intervention for diabetes management. However, more study is needed to investigate the underlying mechanisms of action as well as to assess the long-term effects and safety profile of GC plant extract in human patients. The results of our study were according to the findings of another study that was performed to determine the Garcinia plant activity and use in the prevention and treatment of metabolic syndrome and it was found that several metabolic syndrome-related actions, including lowering body fat mass, blood sugar levels, body weight, total cholesterol, and triglyceride levels. These effects were linked to the suppression of metabolic syndrome-associated enzymes and pathways such as fatty acid synthase, -amylase, and –glucosidase[18]. Similarly in another study the researchers were aimed to look into the therapeutic benefits of Garcinia cambogia (Garcinia cambogia) on glucose homeostasis in obese-induced diabetes, as well as the underlying processes. C2C12 myotubes and mice given a high-fat diet (HFD) were used in the tests. They discovered that Garcinia cambogia therapy boosted glucose absorption in myotubes and activated glucose metabolism signaling pathways such as AMPK, ACC, and MAPK activation. Garcinia cambogia also increased intracellular calcium levels, which activated CaMKII and TBC1D4-mediated GLUT4 translocation, facilitating glucose absorption. Furthermore, Garcinia cambogia supplementation resulted in substantial decreases in blood glucose levels in HFD-induced diabetic rats[19].

CONCLUSION

The study suggests that Garcinia Cambogia plant extract has favourable benefits on blood glucose levels and glycemic control in an animal model of type 2 diabetes, especially at higher dosages. These findings support the use of old medicine techniques, such as herbal treatments, in the treatment of type 2 diabetes. However, more study is required to verify these findings and investigate the underlying mechanisms of action. It should be noted that this study was done in an animal model, and the results reported in rats may not be directly applicable to human population. As a result, when applying these findings to clinical practice, care should be used.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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