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The effects of three different dosages of Garcinia Cambogia Extract on the atherogenic index of plasma (AIP) and insulin gene expression in T2DM Albino Wistar rats

[1]Prof. Dr Kashif Rasheed Shaikh, [2]Prof. Dr Kausar Amir, [3]Dr. Shomail Saeed Siddiqui

[1]Professor, Department of Pharmacology, Suleman Roshan Medical College, Tando Adam, Sindh, Pakistan, drkrs1985@gmail.com
[2]Professor, Department of Pharmacology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center Karachi, Sindh, Pakistan, kausar25@gmail.com
[3]Associate professor, Department of Pathology, Indus Medical College, Tando Muhammad Khan siddiquishomail@gmail.com

Correspondence Author: Prof Dr Kashif Rasheed Shaikh, Email: drkrs1985@gmail.com

Abstract

Introduction
The purpose of this study is to see how Garcinia Camobogia affects the Atherogenic Index of plasma and insulin gene expression in alloxan-induced albino Wistar rats.
Methodology
Albino Wistar rats were obtained from the Open Market/Animal House of the JPMC Karachi Basic Medical Sciences Institute. The researchers followed the standards specified in the NIH Guide for the Care and Use of Laboratory Animals to ensure sufficient housing and treatment of the rats. The rats were housed in stainless steel cages with sawdust bedding, stainless steel feed containers, and plastic drinking bottles with stainless steel nozzles.
Results
GcE therapy significantly reduced the Atherogenic Index of Plasma (AIP), indicating improved lipid profiles and lower cardiovascular risk. Furthermore, as compared to the positive control group, GcE treatment increased insulin gene expression significantly. These findings suggest that GcE has therapeutic potential for decreasing cardiovascular risk factors and increasing insulin secretion and function.
Conclusion
The study discovered that GcE treatment resulted in significant reductions in the Atherogenic Index of Plasma (AIP), implying improved lipid profiles and decreased cardiovascular risk. Furthermore, GcE therapy increased insulin gene expression when compared to the positive control group, indicating potential benefits for insulin synthesis and function.
Keywords
Diabetes Mellitus, Insulin, Cholesterol

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Introduction

Garcinia cambogia (GC), a plant species native to Southeast Asia and India, has piqued the interest of researchers because of its potential influence on a range of health conditions, including Type 2 Diabetes Mellitus1. This plant is well-known for its high content of hydroxycitric acid (HCA), particularly the isomer ()-hydroxycitric acid, which has been connected to a variety of health advantages. Garcinia cambogia can lower blood lipids, which is one of its effects in relation to Type 2 Diabetes Mellitus. High levels of blood lipids, such as cholesterol and triglycerides, are common in diabetics and can contribute to cardiovascular problems[2-3]. Garcinia cambogia HCA has been proven to help reduce lipid levels, which may be effective in the treatment of diabetes and its complications. Garcinia cambogia's anti-diabetic potential has also been investigated.4-6. Garcinia cambogia HCA has been proven to have an effect on serotonin, a neurotransmitter implicated in appetite management and fullness7-8. Garcinia cambogia may help reduce food consumption and increase feelings of fullness by influencing serotonin levels, so aiding diabetics' weight control. Garcinia cambogia also contains HCA, which has been proven to inhibit the enzyme ATP citrate lyase (ATP citrate lyase).[9]. This enzyme is required for fatty acid, cholesterol, and triglyceride synthesis. Garcinia cambogia may help reduce fat formation in the body by inhibiting ATP citrate lyase, which may be beneficial for diabetics who are predisposed to obesity and its complications.[10-12]. A study is performed to determine the effects of GC water extract on insulin resistance and hepatic lipid accumulation in high fat diet mice, it has benn found that Garcinia cambogia can help with insulin resistance, which is a major contributor in the development and progression of NAFLD[13]. Garcinia cambogia may help manage blood sugar levels and lower the strain on the liver by enhancing insulin sensitivity, potentially decreasing hepatic lipid buildup and accompanying liver damage. While there is some evidence showing that Garcinia cambogia may have some advantages for Type 2 Diabetes Mellitus, additional study is needed to completely evaluate its usefulness and develop proper dose recommendations. Before beginning any new supplement or making any modifications to your diabetes treatment regimen, please consult with a healthcare practitioner. Hence therefore the present study has been aimed to determine the Garcinia Camobogia dose response effects on Atherogenic Index of plasma and insulin gene expression among alloxan induced albino Wistar rats.

Methodology

Study Design: The investigation was carried out as an animal experimental study.

Study Setting: The study was conducted at the Animal House in conjunction with the Department of Pharmacology and Therapeutics at the Basic Medical Sciences Institute at JPMC Karachi.

Animal Housing: Albino Wistar rats were procured from the JPMC Karachi Basic Medical Sciences Institute's Open Market/Animal House. To guarantee adequate housing and treatment of the rats, the researchers followed 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 stainless steel nozzles on plastic drinking bottles. The housing environment was clean and well-ventilated, and the rats had unlimited access to laboratory food and tap water. To simulate the natural day-night cycle, a 12-hour light-dark cycle was maintained.

Experimental Protocol

The experimental protocol consisted of 100 Wistar rats split into five groups of ten rats each.

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

Groups of Experimenters: Diabetes mellitus was produced in Group B (n=20) by intraperitoneal injection of Alloxan at a dosage of 120 mg/kg body weight.

Diabetic rats were given Garcinia cambogia extract (GcE) at a dose of 25 g/kg body weight daily for 8 weeks in Group C (n=20).

Diabetic rats were given Garcinia cambogia extract (GcE) at a dose of 50 g/kg body weight daily for 8 weeks in Group D (n=20).

Diabetic rats were given 75 g/kg body weight of Garcinia cambogia extract (GcE) daily for 8 weeks in Group E (n=20).

Wilshire Pharmaceuticals Pakistan provided the Garcinia cambogia extract used in the trial, called G-Lite, which contains (-)-hydroxycitric acid (HCA). The HCA levels in Garcinia cambogia extract were similar to 1000, 2000, and 3000 mg/kg of GcE, respectively. The product's batch number, manufacture date, and expiry date were meticulously confirmed.
The researchers used this experimental methodology to study the effects of different dosages of Garcinia cambogia extract on diabetic rats over an 8-week period.

Outcome Measures
Atherogenic Index of Plasma (AIP)
AIP was measured using enzymatic tests to determine the amounts of total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) in plasma samples[14].
The following AIP values were computed and interpreted as;
0.3 to 0.1 are linked with minimal cardiovascular risk.
0.1 to 0.24 for low cardiovascular risk and
>0.24 for severe cardiovascular risk
Insulin Gene Expression
Following the collection of blood samples, diabetic rats were euthanized by cervical dislocation during the 8th week post-experiment period[15]. Following a laparotomy surgery, pancreatic tissue was immediately extracted. The tissue was carefully divided into 3 to 5 mm diameter sections and transferred to RNAse-free Eppendorf tubes. The samples were instantly frozen in liquid nitrogen and then kept at -80°C until further analysis to maintain RNA integrity. To avoid RNA degradation, the specimen was harvested on ice, and all surgical equipment were proven to be RNAse-free. These steps were taken to make it easier to isolate RNA from pancreatic tissue. RNA extraction enables the study of gene expression, including the expression of the insulin gene. The pancreatic tissue samples obtained might be utilised to investigate changes in insulin gene expression levels, which could provide insight into the influence of Garcinia cambogia extract on insulin regulation in diabetic rats. Analysing insulin gene expression might help evaluate the probable processes through which Garcinia cambogia may exert its benefits on diabetes control.
Results
The findings revealed that the experimental groups treated with Garcinia cambogia extract (GcE), namely groups C, D, and E, saw significant reductions in the Atherogenic Index of Plasma (AIP). These groups' AIP values were 0.662±0.115, 0.617±0.091, and 0.488±0.145, respectively. In comparison, the AIP value for the positive control group (group B) was 1.150.158. The statistical analysis revealed that the observed differences in AIP values between the experimental groups and the positive control group were extremely significant (F-value = 162.7, P < 0.0001). Furthermore, the AIP value for the negative control group (group A) was 0.17±0.089, as shown in Table 1. This means that the experimental groups treated with GcE outperformed the untreated positive control group (group B) in terms of AIP. The considerable decreases in AIP imply that GcE may be useful in the management of atherogenic risk factors associated with cardiovascular disease. A lower AIP score indicates a better lipid profile since it represents a reduction in the plasma ratio of atherogenic to anti-atherogenic lipids. These data support the idea that GcE therapy may help to alleviate AIP and enhance lipid profiles in diabetic rats. The reduction in AIP demonstrates Garcinia cambogia's potential as a therapeutic intervention for reducing cardiovascular risk factors in the setting of diabetes (table 1).

Table 1 Atherogenic Index of Plasma

Variables	Mean	SD	F-value	p-value
Group A	0.179	0.089	162.7	0.0001
Group B	1.15	0.158		
Group C	0.662	0.115		
Group D	0.617	0.091		
Group E	0.488	0.145		

In addition to that the insulin gene expression was measured and quantified, as shown in Table 2. The mRNA amount for the insulin gene was determined to be 1.000.00 in the negative control group (group A). This mRNA amount was dramatically reduced in the positive control group (group B), measured 0.482±0.303. Notably, the insulin gene expression was considerably greater in the GcE-treated experimental groups, namely groups C, D, and E. The mRNA amounts in these groups were 12.950.935, 14.4320.895, and 17.0201.402, respectively. These results showed a significant increase in insulin gene expression when compared to the untreated positive control group (group B). With an F-value of 1646.7 and a P-value of 0.0001, the statistical analysis verified the extremely significant differences between the GcE-treated experimental groups and the positive control group. The considerable increase of insulin gene expression in the GcE-treated experimental groups suggests that Garcinia cambogia extract has the ability to promote insulin production. This data implies that GcE may play a role in increasing insulin secretion and function, which is critical in diabetes care.

Table 1 Insulin Gene Expression mRNA

Variables	Mean	SD	F-value	p-value
Group A	1	0.00	1646.7	0.001
Group B	0.482	0.303		
Group C	12.955	0.935		
Group D	14.432	0.895		
Group E	17.02	1.402		

Discussion

The findings of this study show that Garcinia cambogia extract (GcE) found beneficial in reducing atherogenic risk factors linked with cardiovascular disease and boosting insulin production. GcE treatment resulted in substantial reductions in the Atherogenic Index of Plasma (AIP), indicating better lipid profiles and lower cardiovascular risk. Furthermore, as compared to the positive control group, GcE therapy resulted in a significant increase in insulin gene expression. These data imply that GcE has therapeutic promise in terms of lowering cardiovascular risk factors and improving insulin secretion and function. The findings were according to the findings of study that were performed with the aim to determine the mechanism of action of Garcinia Cambogia as well as its adjuvant function in weight reduction and the treatment of type 2 diabetes, dyslipidemia, and hypertension[16]. It was found by the authors that Garcinia cambogia and its active component, hydroxycitric acid, have been shown to be beneficial as herbal medicine in the treatment of obesity. These therapies have been shown to induce lower glucose absorption, reduced appetite, and a better lipid profile. Significant effects have been found, especially when accompanied with regular physical exercise. Garcinia cambogia's adjuvant function in the treatment of type 2 diabetes, hypertension, and dyslipidemia is ascribed to its capacity to regulate body weight, which leads to improvements in lipid, glycemic, and blood pressure indicators. Garcinia cambogia may help to the general improvement of these health factors by assisting with weight control[17]. Similarly in another study that was performed with the aim to determine the potential role of Garcinia family as anti-metabolic syndrome it was found that various Garcinia species, including Garcinia cambogia, Garcinia atroviridis, Garcinia indica, Garcinia brasilines, Garcinia mangostana, and Garcinia handbury, have bioactivity and pharmacological properties that make them potential candidates for treating metabolic syndrome[18]. These qualities largely target disorders such as obesity and hyperlipidemia, and they work through a variety of processes and routes. Further the Garcinia species' bioactive components have showed promise in modifying metabolic processes involved with metabolic syndrome. They help with weight loss by reducing fat formation, decreasing adipogenesis, and

lowering hunger. Furthermore, these substances have been shown to enhance lipid profiles by lowering triglyceride, total cholesterol, and low-density lipoprotein cholesterol levels while boosting high-density lipoprotein cholesterol levels[19]. While conducting the study we have come across some strength and limitations accordingly the strength of this study is the utilization of an animal experimental design, which allows for controlled testing and analysis of the effects of Garcinia cambogia extract, is one of the study's benefits. Multiple experimental groups and a negative control group were included, allowing for the comparison and assessment of varied extract dosages. The Atherogenic Index of Plasma (AIP) and insulin gene expression were assessed as critical outcomes for evaluating cardiovascular risk factors and insulin control in diabetes. However, some constraints to consider as limitations as the study was done on albino Wistar rats, hence the results may not be applicable to human populations. More study with human volunteers is required to corroborate the reported effects. Furthermore, the very small sample size of 10 rats per group may restrict the data' generalizability. In addition to that the research concentrated on the impact of Garcinia cambogia extract on particular outcomes linked to atherogenic risk factors and insulin gene expression. More researches are needed to determine the influence of Garcinia cambogia on other areas of diabetes management and metabolic syndrome.

Conclusion

In conclusion, the outcomes of this study suggest that Garcinia cambogia extract (GcE) has the ability to reduce atherogenic risk factors linked with cardiovascular disease and improve insulin production. The study found that GcE therapy resulted in substantial decreases in the Atherogenic Index of Plasma (AIP), suggesting better lipid profiles and lower cardiovascular risk. Furthermore, as compared to the positive control group, GcE treatment enhanced insulin gene expression, indicating potential advantages for insulin production and function. These findings are consistent with earlier research on Garcinia cambogia's mode of action and its involvement in weight loss and the treatment of illnesses such as type 2 diabetes, dyslipidemia, and hypertension. Garcinia cambogia's key ingredient, hydroxycitric acid, has shown encouraging benefits in the treatment of obesity by lowering glucose absorption, controlling hunger, and improving lipid profiles. The potential of Garcinia cambogia to manage body weight, resulting to improvements in glycemic control, cholesterol levels, and blood pressure, may explain its adjuvant function in the treatment of metabolic syndrome, which includes type 2 diabetes, hypertension, and dyslipidemia.

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