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# Dose-Response effect of Garcinia Cambogia extracts on Blood Urea Nitrogen (BUN) and Serum Creatinine levels among Alloxan Induced Diabetic Rats

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## Abstract

### Introduction

As a possible medication for Diabetes Mellitus (DM) and its consequences, the natural supplement garcinia cambogia shows promise. In this respect, the goal of the current study is to examine the possible impacts of various Garcinia cambogia (GC) dosages on the levels of serum creatinine (SC) and blood urea nitrogen (BUN) in Alloxan-induced diabetic rats.

### Methodology

Rats were kept in stainless steel cages with sawdust bedding, stainless steel feed containers, and plastic drinks with stainless nozzles. The light/dark cycle was kept at 12-hour intervals, and they were given access to lab food and water at will. The NIH Guide for the Care and Use of Laboratory Animals was followed for housing and handling the animals.

### Results

The treated experimental groups, group C (19.28±1.68 mg/dl), group D (18.48±1.54 mg/dl), and group E (14.27±2.43 mg/dl), all showed a notable decrease in blood urea nitrogen (BUN) levels. Contrastingly, the positive control group B showed a considerably higher BUN level of 23.63±3.04 mg/ml compared to the negative control group A's BUN level of 8.43±0.69 mg/ml. The statistical significance of this difference was unusually high (F-value = 158.3 and P = 0.0001).

### Conclusion

The results show that the GcE-treated experimental groups (C, D, and E) had significantly lower blood urea nitrogen (BUN) levels than the positive control group (B) that was not given any treatment. The

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study also shows that these GcE-treated groups had significantly lower serum creatinine (SCr) levels, which supports the beneficial effects of GcE on renal function even further.

**Keywords**
Diabetes Mellitus, Serum Creatinine, Blood Urea Nitrogen

## Introduction

Diabetes Mellitus (DM) is a common metabolic condition marked by persistently high blood glucose levels brought on by the improper metabolism of food elements such carbs, lipids, and proteins[1]. The main cause of this syndrome is either a whole or partial lack of insulin secretion or action, or a combination of these two causes[2]. According to the World Health Organization (WHO), diabetes affects 422 million people worldwide, making it a serious public health issue not just in industrialized nations but also in developing countries like Pakistan[3-4]. About 43% of people who have diabetes die prematurely, especially those who are between the ages of 40 and 65, who are considered to be working age. Sedentary habits, a lack of exercise, and the consumption of poor diets, such as fast food heavy in fat and carbohydrates, all contribute to this worrying trend[5]. Due to these causes, it is predicted that the number of diabetes cases might quadruple by 2045, with developing nations alone seeing a significant increase from 26 million cases in 1990 to 65 million cases in 2016[5-6].Blood urea nitrogen (BUN) and serum creatinine are two crucial indications in the setting of diabetes that are crucial for diagnosing and treating the condition[7-8]. One of the most prevalent problems among older diabetes patients is diabetic nephropathy, which may be detected early with the use of these measures[9]. Diabetic nephropathy causes

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widespread scarring and entails gradual kidney injury that mostly affects the capillaries in the glomeruli. BUN, serum creatinine, creatinine clearance, urine albumin, and glomerular filtration rate (GFR) measures are frequently used to evaluate renal function in diabetics, albeit a biopsy may be necessary for a conclusive diagnosis[10-11]. Notably, urine microalbuminuria (>300 mg/dL), a decrease in GFR, and a higher risk of cardiovascular morbidity and death are all signs of diabetic nephropathy[12-13]. When assessing the health of the kidneys in people with diabetes, BUN and serum creatinine levels are particularly important. These tests are easily accessible and may be used on a regular basis, making it possible to identify kidney involvement early and perhaps stop the course of end-stage renal disease by prompt therapies[14]. Higher insulin resistance and the inhibition of insulin production have been associated to higher urea levels, as measured by BUN. Furthermore, a greater risk of diabetes mellitus has been linked to BUN levels above 25 mg/dL. On the other hand, because of its relatively constant concentration and reflection of skeletal muscle mass, serum creatinine functions as a sensitive measure of renal involvement in diabetes[15-16]. Creatinine concentration is a sign of renal function as opposed to BUN, which involves reabsorption in the nephron tubules and less sensitive to variations in GFR. As a possible medication for Diabetes Mellitus (DM) and its consequences, the natural supplement garcinia cambogia shows promise. In this respect, the goal of the current study is to examine the possible impacts of various Garcinia cambogia (GC) dosages on the levels of serum creatinine (SC) and blood urea nitrogen (BUN) in Alloxan-induced diabetic rats.

**Methodology**

**Study Design:**

An animal experimentation design is used in this investigation.

**Study Setting**

The study was carried out at the Animal House in Karachi in association with the Basic Medical Sciences Institute at the Jinnah Postgraduate Medical Centre (JPMC), Department of Pharmacology and Therapeutics. A total on n=100 rats were recruited in the study.

**Inclusion/Exclusion Criteria**

Adult male albino Wistar rats weighing between 150 and 200 grams on average were included. Female and ill rats were excluded from the study.

**Animal Housing and Feeding**

Rats were kept in stainless steel cages with sawdust bedding, stainless steel feed containers, and plastic drinks with stainless nozzles. The light/dark cycle was kept at 12-hour intervals, and they were given access to lab food and water at will. The NIH Guide for the Care and Use of Laboratory Animals was followed for housing and handling the animals.

**Administration of Alloxan**

After an overnight fast, rats were given intraperitoneal injections of Alloxan monohydrate (Sigma Aldrich) to induce diabetes mellitus. Diabetes was induced with a single dosage of Alloxan (120 mg/kg body weight) dissolved in sterile saline.

**Animal Grouping**

Rats were group into five (n=20 rats in each group), as follows:

**Group A**

Rats in the control group were given a placebo of 0.9% normal saline.

**Groups B**

Rats with diabetes

**Group C**

Included diabetic rats that received Garcinia Cambogia Extract (GcE) treatment for eight weeks at a dose of 25 g/kg body weight per day.

**Group D**

Diabetic Rats received GcE treatment every day for eight weeks at a dosage of 50 g/kg body weight.

**Group E**

Consists of diabetic rats that received GcE treatment at a dosage of 75 g/kg daily for 8 weeks.

**Outcome Measures**

The levels of serum creatinine (SCr) and blood urea nitrogen (BUN) in the rats served as the study's main outcome indicators. Standard biochemical techniques were used to evaluate these characteristics. While SCr levels were assessed using a colorimetric assay based on Jaffe's reaction, BUN levels were calculated using the Urease-Glutamate Dehydrogenase (GDH) technique. Anesthesia was delivered 24 hours before the collection of serum samples, and the measurements were performed at the conclusion of the 8-week study period.

**Results**

The baseline body weights of both the control and experimental rats were diligently examined, and it was discovered that they were very stable across both groups. This remarkable consistency is supported by a miniscule P-value (P = 0.57), indicating unambiguously that there was no significant difference in the initial body weights across the four rat groups. The homogeneity in baseline body weights acts as a cornerstone in reducing any potential research bias, providing a setting favorable to rigorous and exact comparison and interpretation of the experimental data. (Table 1)

**Table 1 Baseline Characteristics of rats in term of Weights measured in grams (between group comparision)**

| 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 | | |

**Effects of different doses of Garcinia Cambogia Extract on the levels of BUN and SCr**

The study's findings provide a convincing account of Garcinia Cambogia Extract (GcE) in improved kidney health. The treated experimental groups, group C (19.28±1.68 mg/dl), group D (18.48±1.54 mg/dl), and group E (14.27±2.43 mg/dl), all showed a notable decrease in blood urea nitrogen (BUN) levels. Contrastingly, the positive control group B showed a considerably higher BUN level of 23.63±3.04 mg/ml compared to the negative control group A's BUN level of 8.43±0.69 mg/ml. The statistical significance of this difference was unusually high (F-value = 158.3 and P = 0.0001). Given that GcE significantly reduced BUN levels in the treated experimental groups as compared to the untreated positive control group B, these results highlight the substantial renal ameliorative effects of GcE (table 2). Further,

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the positive control group B had a serum creatinine (SCr) level of 5.06±1.40 mg/ml. GcE-treated experimental groups, on the other hand, showed a significant drop in SCr levels: group C (4.84±1.52 mg/dl), group D (3.47±0.40 mg/dl), and group E (3.29±0.52 mg/dl). The SCr level in negative control group A, on the other hand, was 0.910.18 mg/ml. This remarkable change in SCr levels was followed by a statistically significant difference (F-value = 57.6 and P = 0.0001). These findings highlight the beneficial effect of GcE on renal function, as indicated by the significant reduction in blood creatinine levels in the treated experimental groups (table 2).

**Table 2Comparative analysis in BUN and SCr levels of rats (Between group Analyses)**

| **Blood, Urea Nitrogen Levels (mg/dl)** | | | |
|---|---|---|---|
| **Variables** | **Mean levls± SD** | **F-Value** | **Level of Significance** |
| **Group A** | 8.43±0.69 | 158.3 | 0.0001 |
| **Group B** | 23.63±3.04 | | |
| **Group C** | 19.28±1.68 | | |
| **Group D** | 18.48±1.54 | | |
| **Group E** | 14.27±2.43 | | |
| **Serum Creatinine Levels (SCr)** | | | |
| **Group A** | 0.91±0.18 | 57.6 | 0.0001 |
| **Group B** | 5.06±1.4 | | |
| **Group C** | 4.84±1.52 | | |
| **Group D** | 3.47±0.4 | | |
| **Group E** | 3.29±0.52 | | |

**Discussion**

The results of the study offer strong proof of Garcinia Cambogia Extract's (GcE) beneficial effects on kidney function. Blood urea nitrogen (BUN) levels in the treated experimental groups (group C: 19.28±1.68 mg/dl, group D: 18.48±1.54 mg/dl, and group E: 14.27±2.43 mg/dl) significantly dropped. This contrasts sharply with the significantly higher BUN level (23.63±3.04 mg/ml) in the positive control group B compared to the BUN level of 8.430.69 mg/ml in the negative control group A. This difference's was statistical significance (F-value = 158.3 and P = 0.0001). Notably, GcE considerably reduced BUN levels in the treated experimental groups as compared to the positive control group B that received no treatment, highlighting the substance's strong renal ameliorative effects. Serum creatinine (SCr) levels in the experimental groups that had received GcE treatment were significantly lower than those in the positive control group B (5.06±1.40 mg/ml), group C (4.84±1.52 mg/dl), group D (3.47±0.40 mg/dl), and group E (3.29±0.52 mg/dl). The SCr level in group A's negative control, in comparison, was 0.91±0.18 mg/ml. This striking change in SCr levels was followed by a statistical difference that was extremely significant (F-value = 57.6 and P = 0.0001). These results highlight the beneficial effects of GcE on renal function, with the treated experimental groups showing a significant decline in blood creatinine levels. A study was conducted with the purpose to look into the effects of Garcinia cambogia (G.C.) peel powder and extract (GCE) on obese rats[16]. A total of n=25 rats were separated into groups after being fed a high-



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fat diet to make them obese. One group served as a positive control, while the other four groups each received varied dosages of G.C. powder or GCE. Several variables were assessed after the treatment period of 28 days. The results showed that obesity produced a substantial drop in HDL cholesterol while increasing body weight gain, feed consumption, blood lipid levels, liver enzymes, uric acid, urea, creatinine, and glucose[16]. The injection of G.C. powder and GCE, however, successfully restored these negative effects. In the High-Fat Diet (HFD) generated obesity paradigm, the study examining the effect of Garcinia cambogia (G. cambogia) on reducing creatinine levels in rats[17]. Eight groups of rats were used in the investigation, and it was shown that HFD-induced obesity caused higher blood urea levels, which suggested nephrotoxicity. Nevertheless, after 42 days of therapy, the groups given Triphala, Garcinia cambogia, or both of them shown a substantial decrease in blood urea levels, thereby reducing the nephrotoxic effects brought on by the HFD[17]. Notably, co-treatment with Triphala and G. cambogia extracts showed a further reduction in blood urea levels, highlighting the potential of G. cambogia and Triphala to safeguard and enhance renal function in the setting of obesity-induced nephrotoxicity. Another study examined the impact of several therapies on Blood Urea Nitrogen (BUN) levels in the setting of a high-fat diet (HFD)-induced obesity paradigm[18]. BUN values in the HFD control group were considerably higher than in the normal control group, indicating the possibility of nephrotoxicity brought on by obesity. Treatments with 250 mg/kgBW doses of Green Tea extract (GT), 250 mg/kgBW doses of Garcinia atroviridis extract (GA), or a combination of GT and GA at the same dosages, however, resulted in a significant decline in BUN levels. The combo therapy, in particular, showed a considerable decline in BUN levels, pointing to a synergistic impact in reducing nephrotoxicity brought on by the HFD[18]. These results demonstrate the potential of these therapies, particularly the GT and GA combination, to improve renal function in the setting of obesity-related nephrotoxicity[18]. The controlled animal experimental design, sufficient sample size, use of standardized measuring procedures, and respect to moral standards for animal care are the study's strong points. Recognizing its drawbacks, such as the absence of direct human data and the brief research period, is crucial. The potential effects of Garcinia Cambogia Extract (GcE) on kidney function in the context of diabetes mellitus should be better understood through additional research, including human clinical trials with longer follow-up periods. This will help close the gap between animal studies and clinical applicability.

**Conclusion**

The results show that the GcE-treated experimental groups (C, D, and E) had significantly lower blood urea nitrogen (BUN) levels than the positive control group (B) that was not given any treatment. The study also shows that these GcE-treated groups had significantly lower serum creatinine (SCr) levels, which supports the beneficial effects of GcE on renal function even further. These findings highlight the therapeutic potential of GcE in treating renal problems brought on by diabetes. However, more investigation—including clinical trials—is required to confirm these results and determine their applicability to human health.

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