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The Effect of Giving Ciplukan (*Physalis angulata* L.) Extract on Serum Albumin Levels of Diabetes Model Rats

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Abstract

Background: Diabetes mellitus is a chronic metabolic disease that frequently leads to microvascular complications, including diabetic nephropathy. This condition is characterized by renal damage that increases urinary albumin loss, which subsequently affects serum albumin levels. *Physalis angulata* L. is known to possess antioxidant, anti-inflammatory, and antifibrotic properties. **Objectives:** This study aimed to determine the effect of *Physalis angulata* L. extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW on serum albumin levels in a diabetic rat model. **Methods:** This study used stored biological materials in the form of serum samples obtained from a previous experimental study involving male Wistar rats. Diabetes had been induced using STZ-NA, and the rats had been divided into five groups: a healthy control group, a diabetic control group, and three diabetic groups receiving *Physalis angulata* L. extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW. Serum albumin levels were measured using the Bromocresol Green method. Data analysis was performed using Welch ANOVA. **Key findings:** The results show that serum albumin levels in the healthy control group, diabetic control group, and treatment groups remain within the normal range of 3.0-5.0 g/dL. Welch ANOVA indicates no statistically significant difference in serum albumin levels among the groups with p-value=0.496 ($p > 0.05$). **Conclusions:** In conclusion, administration of *Physalis angulata* L. extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW does not affect serum albumin levels in diabetic rats.

Keywords: Albumin, diabetes mellitus, diabetic nephropathy, *Physalis angulata* L. extract

Introduction

Diabetes mellitus is a chronic metabolic disease characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both, and its prevalence continues to increase globally [1-2]. Chronic hyperglycaemia in diabetes mellitus plays a crucial role in the development of microvascular complications, one of which is diabetic nephropathy, the leading cause of end-stage renal disease in diabetic patients [1,3]. Diabetic nephropathy is characterized by glomerular damage that causes increased permeability of the renal filtration membrane, allowing proteins, particularly albumin, to be easily excreted through the urine.

Albumin is the primary plasma protein that plays a role in maintaining colloid osmotic pressure and acts as a transport protein for various essential substances in circulation. Persistent loss of albumin through urine in diabetic nephropathy can lead to a decrease in serum albumin levels [4,5]. Therefore, serum albumin levels can be used as a biochemical parameter reflecting impaired renal function and metabolic conditions in diabetes mellitus. In animal studies, serum albumin testing is considered more practical and stable compared to urine albumin testing and causes minimal stress to the research animals [6].

The development of diabetic nephropathy involves various pathophysiological mechanisms, including oxidative stress, chronic inflammation, and the activation of profibrotic pathways due to persistent hyperglycaemia [7]. These conditions encourage the development of supportive therapies based on natural ingredients that focus not only on blood glucose control but also on protective effects against target organ damage. The Ciplukan plant (*Physalis angulata* L.) is a herbal plant known to contain bioactive compounds such as flavonoids, alkaloids, saponins, physalins, and phytosterols, which possess antioxidant, anti-inflammatory, and anti-fibrotic activities [8,9].

Previous research has shown that Ciplukan extract is capable of lowering blood glucose levels in diabetic rat models, particularly at doses of 150 mg/kgBW and 300 mg/kgBW [9,10]. Furthermore, the administration of Ciplukan extract has also been reported to improve renal histopathology in diabetic rats, indicating a potential nephroprotective effect [11]. However, research specifically evaluating the effect of Ciplukan extract on serum albumin levels as a biochemical parameter in diabetic rat models is still very limited.

Based on the literature review conducted, there has been no research assessing the effect of Ciplukan (*Physalis angulata* L.) extract administration on serum albumin levels in diabetic rat models induced by streptozotocin–nicotinamide. Therefore, this study possesses an element of novelty by evaluating serum albumin levels as a biochemical indicator reflecting metabolic conditions and renal function in a diabetes model. This study aims to determine the effect of Ciplukan extract doses of 75

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mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW on the serum albumin levels of diabetic rat models. A limitation of this study is the use of a post-test-only design and a relatively short duration of diabetes exposure, such that chronic complications like diabetic nephropathy may not have fully developed and may not yet significantly affect albumin levels.

Materials and Methods

This research utilizes stored biological materials (SBM) in the form of serum samples from a previous study titled "The Effect of Ciplukan (*Physalis angulata* L.) Extract on mRNA and Histopathology of Diabetic Rat Models." The research method used in the previous study was a true experimental laboratory design with a post-test-only control group design. In that study, various laboratory parameters were measured after the administration of Ciplukan extract to 30 male white rats (*Rattus norvegicus*) of the Wistar strain, selected according to inclusion and exclusion criteria using a Completely Randomized Design (CRD). In the present study, serum albumin levels were measured using DiaSys reagents with the Bromocresol Green (BCG) method.

Tools and Materials

The tools used in this study include small test tubes, micropipettes, blue tips, white tips, and a spectrophotometer. The materials used in this study are stored biological materials in the form of rat blood serum samples and DiaSys reagents. A total of 25 serum samples were used because, in the previous study, one rat in group B died due to STZ-NA exposure; therefore, the number of samples was equalized to 5 samples per group.

Research Procedures

The sequence of work in this research began with the ethical submission process, where the study was submitted to and obtained approval from the Research Ethics Committee of the Faculty of Medicine, Jenderal Soedirman University, prior to its implementation. For sample preparation, the study utilized stored biological materials in the form of Wistar strain white rat (*Rattus norvegicus*) serum that had been stored at -80°C. These serum samples were removed from the freezer and allowed to thaw at room temperature before being categorized according to the research design into five groups: a healthy control group, a diabetes control group, and three treatment groups receiving Ciplukan extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW, totalling 25 samples.

The measurement of serum albumin levels was then performed using the Bromocresol Green (BCG) method with a spectrophotometer at a wavelength of 546 nm. Commercial reagents were used strictly according to the manufacturer's instructions, where the serum was mixed with the reagent and incubated at room temperature before the absorbance was read to obtain the concentration values. Throughout the process, all stages of the research and examination results were documented as part of the formal recording and reporting. Finally, the data from the serum albumin level measurements were analysed using Statistical Product and Service Solution (SPSS) software to assess the statistical differences between the research groups.

Data Analysis

Univariate analysis was conducted to determine the mean and standard deviation data from the research results of albumin levels across the 5 tested rat groups. Bivariate analysis was conducted to compare the effect of giving Ciplukan (*Physalis angulata* L.) extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW on the serum albumin levels of diabetic rat models. The Shapiro-Wilk normality test showed that the data were normally distributed, while the Levene's Test for homogeneity of variance showed that the data were not homogeneous. Because the data were normally distributed but had non-homogeneous variances, the analysis proceeded with the Welch ANOVA, which is an alternative to ANOVA specifically designed for data that are normally distributed but lack homogeneity of variance. The Welch ANOVA test showed a p-value >0.05, meaning there were no significant differences between groups; therefore, no Post Hoc tests were performed.

Results and Discussion

This study evaluated serum albumin levels in male Wistar white rats divided into five groups: a healthy control group, a diabetes control group, and three groups of diabetic rat models treated with Ciplukan (*Physalis angulata* L.) extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW. Serum albumin level testing was conducted using the Bromocresol Green (BCG) method.

The results of the serum albumin measurements indicated that all groups had albumin values within the normal range for rats, which is 3.0–5.0 g/dL. The mean serum albumin levels for each group are presented in Table I. Statistical analysis using the Welch ANOVA test showed that there were no significant differences in serum albumin levels between the healthy control group, the diabetes control group, or the treatment groups receiving various doses of Ciplukan extract ($p = 0.496$; $p > 0.05$\$).

The absence of significant differences in serum albumin levels between groups indicates that the induction of diabetes using streptozotocin–nicotinamide (STZ-NA) in this study had not yet caused a systemic decrease in serum albumin levels. The STZ-NA model is known to produce a type 2 diabetes condition with partial damage to pancreatic beta-cells, which does not always result in severe diabetic nephropathy complications within a short period [12].

Furthermore, serum albumin levels are influenced by various factors, including hepatic function as the site of albumin synthesis, nutritional status, and the severity of kidney damage. In this study, although the rats were in a diabetic state, the albumin synthesis function of the liver is presumed to have remained adequate, keeping serum albumin levels within normal limits. This aligns with the theory that a decrease in serum albumin levels generally occurs in advanced diabetic nephropathy or in conditions of severe and persistent albuminuria [4,5].

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Table 1. Rat Serum Albumin Levels Across Various Treatment Groups

Group (n=5)	Mean ± SD (g/dL)	*Saphiro Wilk*	*Lavene Test*	*Welch ANOVA*
A	3,19 ± 0,43	0,974		
B	4,91 ± 1,93	0,932		
C	3,60 ± 0,40	0,955	0,000	0,406
D	3,34 ± 0,25	0,970		
E	3,34 ± 1,65	0,919		

The administration of Ciplukan (*Physalis angulata* L.) extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW also showed no significant increase or decrease in serum albumin levels. This may be due to the duration of the study not being long enough to cause biochemical changes in serum albumin, or because the protective effects of Ciplukan may play a more significant role at the structural and molecular levels of the kidney rather than through direct changes in serum albumin levels.

The results of this study are consistent with several previous studies reporting that serum albumin levels in diabetic rat models do not always experience a significant decrease, especially in the early stages or mild degrees of diabetic nephropathy. Syavamaruah et al. (2025) reported that in patients with type 2 diabetes mellitus, serum albumin levels do not always correlate directly with the duration of diabetes, particularly if severe kidney damage has not yet occurred [13].

Research by Nwankwo and Oluka (2023) investigating the effect of *Physalis angulata* extract on normal rats also showed that the administration of Ciplukan extract did not cause significant changes in serum albumin levels, indicating that this plant is relatively safe regarding plasma protein synthesis function [14]. This supports the findings of this study that Ciplukan extract does not lower serum albumin levels.

On the other hand, several other studies have reported that Ciplukan has nephroprotective effects demonstrated through improvements in renal histopathology or reductions in other kidney damage parameters. Sulistyowati et al. (2024) showed an improvement in the number of glomeruli experiencing diabetic nephropathy in diabetic rats after the administration of Ciplukan extract, while other studies have reported that Ciplukan extract has no effect on serum creatinine levels [11]. These differences in results are likely caused by variations in the parameters evaluated, the duration of treatment, and the severity of diabetic nephropathy in each study.

Thus, the lack of influence of Ciplukan extract on serum albumin levels in this study does not negate the potential benefits of Ciplukan in diabetes mellitus. Instead, it suggests that serum albumin may not be the most sensitive parameter for detecting the nephroprotective effects of Ciplukan in the early stages of diabetes. Evaluations of other parameters, such as Neutrophil Gelatinase-Associated Lipocalin (NGAL) or renal histopathology, are necessary to describe the effects of Ciplukan more comprehensively.

Conclusion

The serum albumin levels in both the healthy control group and the diseased control group (diabetic rat models) were within the normal range, indicating that the diabetic condition in this research model had not yet caused systemic serum albumin disturbances. The administration of Ciplukan (*Physalis angulata* L.) extract at doses of 75 mg/kgBW, 150 mg/kgBW, and 300 mg/kgBW also resulted in serum albumin levels that remained within the normal range and did not exert any influence on the serum albumin levels of the diabetic rat models. Consequently, this study did not find an effective dose of Ciplukan extract to increase serum albumin levels in diabetic rat models. These findings provide scientific justification that Ciplukan extract does not disrupt serum albumin homeostasis and is potentially safe as a supportive therapy; however, further research with more sensitive renal parameters, longer treatment durations, and histopathological and molecular approaches is required to evaluate its nephroprotective potential more comprehensively.

Supplementary Material

None

Author Contributions

FN : Conceptualization, Methodology, Writing-Original Draft. **WS** : Data Curation, Formal Analysis, Visualization. **IMH** : Supervision, Funding Acquisition, Writing- Review & Editing.

Conflict of Interest

The authors have no financial conflicts of interest to declare.

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