American Journal of Biology and Natural Sciences
https://biojournals.us/index.php/AJBNS
ISSN: 2997-7185

Comparative Study between Drug and Plant Extract for Treatment of Diabetes in Rats

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Received: 2024, 15, Feb
Accepted: 2025, 21, Mar
Published: 2025, 22, Apr

Annotation: The present study was designed for knowledge the comparative study between drug and plant extract for treatment of Diabetes in rats. Cashew that had fully developed and dried in the shade were gathered, cleaned, and crushed into a coarse powder. Using a Soxhlet extractor and ethanol, extracts was done. STZ was administered once at a dosage of 70 mg/kg body weight for the induction of DM. For rats that had been fasting overnight, intraperitoneal injections were utilized, and all treated rats were given access to food and drink. Additionally, fasting blood glucose levels were calculated after 4 days of stabilization for the rats. As a diabetic model, rats with glycemia levels higher than 17 mmol/L were used in the study. Forty adult male rats were used in this study, these were divided into 4 groups. G1 negative control, G2 given STZ only (positive control), G3 given STZ and then treated by Glimepiride (5 mg/10 ml)+ Atorvastatin 10 mg/kg , G4 given STZ and then treated by Cashew extract at 100 mg/kg. Rats were fasted for eight hours after five weeks. Diethyl ether was used to anesthetize the rats, and blood samples were

taken at days 0,7,14,21. The serum samples were maintained at -80°C after the blood serum was separated. The levels of a few biochemical parameters, such as glucose, the lipid profile as well as liver function tests (ALT and AST) which purchased from Biolabo company. More significant ($p < 0.05$) anti-diabetic activity was observed for drugs and cashew extracts, which shows significant gradual decrease in blood glucose levels, TG, C, AST and ALT in both G3 and G4, while HDL was increase significantly after treatment with drugs and cashew extract.

In conclusion, cashew have significant role in control of diabetes by decreasing blood glucose levels, TG, C, AST and ALT and increasing in HDL.

Keywords: Cashew, diabetes, STZ.

Introduction:

Diabetes mellitus (DM) is one of the most common illnesses in the world. Diabetes mellitus (DM) is a chronic condition brought on by a hereditary, acquired, or ineffective pancreatic insulin production system [1]. Multiple pathophysiological problems as well as anomalies in metabolism, proteins, lipids, and carbohydrates are characteristics of DM [2-4]. It is clear that this condition causes hyperglycemia as well as a wide range of other problems, including hyperlipidemia, atherosclerosis, hypertension, neuropathy, retinopathy, as well as nephropathy [5–9]. The increasing prevalence of DM is influenced by a number of variables, including changes in people's lifestyles, behaviors, and environments [10]. The WHO predicts that DM will become more prevalent globally and that 300 million additional people will have it by 2025 [11]. The proportion of DM in the Kingdom of Saudi Arabia is among the highest in the world.

When used therapeutically, medicinal plants offer several advantages, including the ability to treat various ailments safely, effectively, and affordably. For DM and associated comorbidities, natural remedies may be an efficient and secure alternative therapy. It is necessary to first test the possible effects of such tactics on relevant animal models. Several medications are used to manage DM, although complete glucose control is seldom attained [12]. The rise in drug costs, the negative side effects of synthetic medications, and the incomplete recovery of diabetes patients treated with chemical hypoglycemic agents have recently encouraged the use of medicinal plants as alternative treatments [13]. Traditional medically based therapy have recently shown a critical role in the management of diabetes [14].

The Anacardiaceae family includes the cashew tree, sometimes referred to by its Latin name, A. occidentale. A. occidentale, sometimes referred to as Darkassou, is commonly cultivated in tropical nations including Malaysia, India, and Brazil and used to treat diabetes mellitus. [15,16]

A. occidentale, popularly known as cashew, is also widely used in ethnopharmacology to treat inflammatory illnesses including arthritis, skin ailments, and diarrhea.[17, 18, 19, 20, 21]

Additionally, it is used to relieve aches and pains and fevers. [22,23,24] Studies on Cashew's hypoglycemia effect in mice and rats have been documented, according to literature reports. [25,26,27] Numerous investigations on the phytochemistry of A. occidentale have been published, and they show the presence of a wide range of substances including glucosides, glucose, and flavonoids. [28,29,30]. It has been documented that rat model testing type 2 diabetes is suitable for the STZ [31].

The present study was designed for knowledge the comparative study between drug and plant extract for treatment of Diabetes in rats.

Materials and Methods:

Cashew that had fully developed and dried in the shade were gathered, cleaned, and crushed into a coarse powder. Using a Soxhlet as well as ethanol with a ratio of 1:6 (g/mL), the samples were extracted. The ethanol extract was dried using a rotary evaporator, and the leftover material was kept in a refrigerator between 2 and 8 °C for use in further investigations.

STZ was given once at 70 mg/kg B.W for the induction of DM. For rats that had been fasting overnight, intraperitoneal injections were utilized, and all treated rats were given access to food and drink. Additionally, fasting blood glucose levels were calculated after 4 days of stabilization for the rats. As a diabetic model, rats with glycemia levels higher than 17 mmol/L were used in the study [8].

Forty adult male rats were used in this study, these were divided into 4 groups. G1 negative control, G2 given STZ only (positive control), G3 given STZ and then treated by Glimepiride (5 mg/10 ml)+ Atorvastatin 10 mg/kg , G4 given STZ and then treated by Cashew extract at 100 mg/kg [32].

Rats were fasted for eight hours after five weeks. Diethyl ether was used to anesthetize the rats, and blood samples were taken at days 0,7,14,21. The serum samples were maintained at -80°C after the blood serum was separated. The levels of a few biochemical parameters, such as glucose, the lipid profile as well as liver function tests (ALT and AST) which purchased from Biolabo company.

SPSS version 23 was used for analysis of data.

Results and Discussions:

More significant ($p < 0.05$) anti-diabetic activity was observed for Glimepiride and cashew extracts, which shows significant gradual decrease in blood glucose levels in both G3 and G4 (Table 1).

Table 1. Glucose levels (mmol/l) at different times of study (Mean ± SE)

Groups	Zero day	Day 7	Day 14	Day 21
G1	5.3±0.2Ab	5.1±0.6Ab	5.13±0.02Ad	5.21±0.1Ac
G2	15.7±1.1Aa	15.1±0.3Aa	15.3±0.8Aa	15.42±0.6Aa
G3	15.27±0.54Aa	12.3±0.01Ba	8.2±0.2Cc	5.42±0.8Dc
G4	15.1±0.06Aa	13.15±0.4Ba	10.6±0.1Cb	6.1±0.03Dbc

Differences between days are denoted by capital letters ($p \leq 0.05$)

Differences between groups are denoted by small letters ($p \leq 0.05$)

It is understood that the medication STZ enters the beta cells by a glucose transporter pathway in the STZ-induced diabetes model. According to reports, STZ causes DNA to become alkylated by releasing large amounts of nitric oxide and nitrosourea, which inhibits the enzyme aconitase.[33] In STZ animal models, the incidence of insulin resistance depends on a number of variables,

including age, dose of STZ, as well as the strain of the animals. In the current investigation, the extracts exhibited statistically significant reduction in the blood glucose levels at p ≤0.05 especially on day 21. Insulin resistance was caused by injection of STZ on the second day of birth at dose level 90 mg kg1.

The serum levels of the TG and C are significantly higher in the diabetes groups (G2, G3, G4) compared to the healthy control group (p≤0.05). Serum levels of TG and C decreased after treatment with cashew extract and atorvastatin pointing to an improvement in liver health (Table 4).

Table 2. Triglyceride and Cholesterol levels at different periods

Groups	Triglyceride (mmol/L)				Cholesterol (mmol/L)			
	Zero day	Day 7	Day 14	Day 21	Zero day	Day 7	Day 14	Day 21
G1	0.52±0.01Ab	0.51±0.03Ac	0.55±0.06Ac	0.5±0.01Ac	0.92±0.01Ab	0.93±0.05Ac	0.91±0.01Ab	0.92±0.01Ab
G2	1.32±0.02Aa	1.36±0.1Aa	1.3±0.09Aa	1.33±0.3Aa	1.47±0.3Aa	1.49±0.1Aa	1.45±0.09Aa	1.41±0.02Aa
G3	1.41±0.1Aa	1.12±0.07Ba	0.9±0.02Cb	0.62±0.03Db	1.42±0.05Aa	1.21±0.1Bb	0.97±0.02Cb	0.91±0.01Cb
G4	1.39±0.01Aa	1.07±0.06Ba	0.85±0.02Cb	0.59±0.07Db	1.39±0.1Aa	1.13±0.01Bb	0.99±0.03Cb	0.93±0.01Cb

Differences between days are denoted by capital letters (p≤0.05)

Differences between groups are denoted by small letters (p≤0.05)

The serum levels of the HDL is significantly lower in the diabetes groups (G2,G3,G4) compared to the healthy control group (p≤0.05). Serum levels of HDL increase after treatment with cashew extract and atorvastatin pointing to an improvement in liver health (Table 3).

Table 3. HDL levels in different groups at different times

Groups	Zero day	Day 7	Day 14	Day 21
G1	1.47±0.1Ab	1.41±0.04Aa	1.46±0.03Aa	1.43±0.3Aa
G2	0.93±0.02Aa	0.91±0.01Ab	0.93±0.02Ac	0.89±0.01Ab
G3	0.96±0.01Ca	1.05±0.06Cb	1.22±0.02Bb	1.46±0.2Aa
G4	0.99±0.01Ca	1.01±0.04Cb	1.28±0.01Bb	1.39±0.03Aa

Differences between days are denoted by capital letters (p≤0.05)

Differences between groups are denoted by small letters (p≤0.05)

It has been shown that free fatty acid levels rise in people with diabetes. The circulating free fatty acids impair endothelial function through a number of channels and processes, including the formation of free radicals, activation of protein kinase C, and worsening of dyslipidemia. [34] An increase in the body's generation of free radicals leads to oxidative stress, which results in micro and macro vascular complications in diabetes. OS and the development of diabetic complications and insulin resistance are closely related. An increase in oxidative stress, together with an increase in free fatty acids as well as blood glucose levels, has a deleterious influence on insulin function and secretion.. [35]

The serum levels of the two enzymes are significantly higher in the diabetes groups (G2,G3,G4) compared to the healthy control group (p≤0.05). This outcome is suggestive of liver damage brought on by hyperglycemia. Serum levels of AST and ALT decreased after treatment with cashew extract and atorvastatin pointing to an improvement in liver health (Table 4).

Table 4. Liver function tests in different groups at different times

Groups	AST (U/L)				ALT (U/L)			
	Zero day	Day 7	Day 14	Day 21	Zero day	Day 7	Day 14	Day 21
G1	45±1.7Ab	44.5±0.3Ab	47.6±2.2Ac	46.2±4.6Ac	4.6±0.03Ab	4.7±0.1Ac	4.5±0.04Ac	4.6±0.3Ac
G2	63.8±4.7Aa	67.3±3.5Aa	65.6±7.4Aa	66.3±1.3Aa	7.1±0.08Aa	7.3±0.6Aa	7.2±0.2Aa	7.3±0.04Aa
G3	65.5±1.4Aa	62.7±1.9Aa	58.1±3.5Bb	53.8±0.4Cb	7.5±0.02Aa	6.9±0.37Ab	6.1±0.04Bb	5.2±0.01Cb
G4	66.1±2.4Aa	61.3±0.3Ba	59.5±2.3Bb	52.4±0.7Cb	7.3±0.01Aa	6.8±0.1Ab	6±0.02Bb	5±0.07Cc

Differences between days are denoted by capital letters (p≤0.05)

Differences between groups are denoted by small letters. ($p \leq 0.05$)

Publications focusing on hepatic damage in STZ-induced diabetic rat models indicate disorientation in the liver cellular structure in diabetic rats. The structural degeneration comprises acidophilic cytoplasm, glycogen accumulation, and the nucleus' position near the cell membrane's edge. Researchers have discovered microvascular vacuolization, necrotic cells, as well as hydropic inflammation in the livers of diabetic rats. [36]

Similar to prior observations, the decrease in the level of these enzymes with treatment by cashew is a marker of the stability of the plasma membrane as well as the repair of liver damage brought on by STZ [37].

Conclusion:

Cashew have significant role in control of diabetes by decreasing blood glucose levels, TG, C, AST and ALT and increasing in HDL.

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