Original Article

The Effect of Thymus Vulgaris Extract on Pharmacological Activity of Acarbose in Diabetic Animal Model

Asma A. Alkafaji and Majid Kadhim Abbas

ABSTRACT

Objective: To investigate the therapeutic effects of acarbose alone and in combination with thymol on oxidative stress, β-cell function, and glycemic control in streptozotocin (STZ)-induced diabetic rats.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the College of Science at Babylon University, Iraq from 15th July 2025 to 14th December 2025.

Methods: Forty male albino rats (180–320 g) were maintained under controlled conditions (22–25°C, 50% humidity, free access to water). After 2 weeks, rats were randomly divided into four groups: negative (A), positive (B), acarbose-treated (C), and acarbose plus thymol-treated (D). After treatment, rats were sacrificed and blood samples were collected for biochemical and inflammatory analyses.

Results: Group B showed decreased superoxide dismutase (0.337±0.091) and C-peptide (863.17±250.14), with increased advanced oxidation protein products (430.37±77.85) and glucose (148±29.71) vs A ($p<0.05$). Group C increased superoxide dismutase (0.554±0.155) and C-peptide (1248.78±303.68) and reduced advanced oxidation protein products (271.42±120.38) and glucose (102.9±12.74) ($p<0.05$). Group D further increased superoxide dismutase (0.615±0.202) and C-peptide (1368.33±277.35) and decreased advanced oxidation protein products (269.74±59.11) and glucose (97±7.46) ($p<0.05$).

Conclusion: Acarbose improves oxidative stress and glycemic status, while thymol provides additional improvement.

Key Words: Effect, Thymus vulgaris extract, Pharmacological activity, Acarbose, Diabetic animal

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INTRODUCTION

Diabetes mellitus is a long standing metabolic condition characterized by sustained elevation in blood glucose levels arising from insufficient insulin secretion, insulin resistance, or both.[1] Persistent hyperglycemia contributes to enhance generation of reactive oxygen species (ROS), which promotes oxidative stress and plays a major role in the development of long- term diabetes complications, including retinopathy, nephropathy, and neuropathy.[2] Oxidative damage influences cellular lipids, proteins, and DNA, and accelerates β-cell dysfunction, and insulin resistance, making the reduction of oxidative stress a key therapeutic aim.[3]

Traditional treatments for DM, such as oral medications and insulin injections, may have certain side effects such as hypoglycemia (especially insulin) and the symptoms of hypoglycemia may include sweating, confusion, anxiety and dizziness. Phytochemicals found in medicinal plants have been found to have hypoglycemic properties, suggesting they may be useful in reducing the risk of hyperglycemia or may be useful in glycemic control.

Alpha-glucosidase inhibitor (acarbose) is group of medication use to control blood glucose level by inhibited a glucosides enzyme located in intestinal brush border, a glucosidase enzyme breaking down carbohydrate in to glucose that can be absorbed and elevated glucose level.[4]

Vegetables, in particular, are a cornerstone of nutritional strategies for both prevention and management of diabetes mellitus because of their unique composition of dietary fiber, antioxidants, vitamins, minerals, and phytochemicals.[5]

Thymus vulgaris (common thyme) is a small aromatic herb from the flowering plant Lamiaceae, which contains volatile oils rich in thymol and carvacol.[6] In addition to various phenolic components (phenolic acid).[7]

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Medicinally, these constituents exhibit antimicrobial, antioxidant, anti-inflammatory capabilities, which have supported the traditional use of thyme in several health conditions, including metabolic diseases.[8]

Thymol, the principal phenolic monoterpene in thyme, demonstrates strong free radical scavenging activity, and has been reported to enhance endogenous antioxidant enzymes such as superoxide dismutase (SOD), and providing significant protection against oxidative and inflammatory injury, Studies have shown that thymol improves lipid profiles, reduces oxidative markers such as advanced oxidation protein products (AOPP), and preserves pancreatic β-cell integrity. Owing to its natural origin, high safety profile, and strong antioxidant capacity, thymol may be used as a complement to conventional antidiabetic drugs.[9]

Combining acarbose with a natural antioxidant, such as thymol, may offer synergistic therapeutic benefits by improving glycemic control while simultaneously enhancing antioxidant defenses. This combination has the potential to reduce oxidative damage, preserve β-cell function (as reflected by c-peptide levels), and mitigate diabetes-related biochemical alterations more effectively than acarbose alone.

METHODS

This experiment was conducted at College of Science at Babylon University, Iraq from 15th July 2025 to 14th December 2025 vide letter No. 4329 dated 6th July 2025 on 40 adults males, which were obtained from the animal facility of the. All rats were maintained under controlled laboratory conditions for two weeks prior to start of the study. The animals were kept in plastic cages (five rats per cage) and maintained under controlled environment, including a temperature (22–25°C), relative humidity of approximately adequate ventilation, and a 12 house light/dark cycle. Following acclimatization, the animals were randomly and manually allocated into four groups, (n=10 per group) (based on prior studies with similar effect sizes, n=10/group was deemed sufficient) using a simple randomization method to ensure unbiased group allocation.

Chemical and reagent: STZ from Heowns (China), acarbose from exit costar (Iran),and thymus vulgaris from natural (India).

Induction of T2DM: To establish the type 2 diabetes mellitus (T2DM) model characterized by increased adiposity, a modified protocol based on was employed, except for the control group, all rats were maintained on a high-fat diet (HFD) supplemented with butter and cholesterol powder for a 14-day pre-induction period to promote fat accumulation. Following an 8–10 hour fast, T2DM was induced via a single intraperitoneal (IP) injection of streptozotocin (STZ) at a dosage of 35 mg/kg prepared by dissolving 100 mg of STZ in 10 ml of normal saline. To ensure stability, the STZ solution was kept refrigerated and shielded from light until the moment of administration. Animals exhibiting fasting blood glucose levels 125 mg/dl were confirmed as diabetic and included in the experimental cohorts.[10]

Experimented design: Fourth adult male rats were randomly divided into 4 groups with ten animals in each group and the experimental animal groups received.

Group A was the negative control group (normal group), which is received distilled water and pellet feed for 12 days and injected with normal saline.

Group B was the positive group that received a high fat diet (cholesterol powder and butter) for 12 days and was then injected with streptozotocin (STZ) at 35mg/kg.[11]

Group C was the diabetic treated group that was injected with STZ (35 mg/kg) and then treated with 24mg/kg of acarbose for 14 days.[12]

Group D was the diabetic treated combination group that was injected with STZ (35 mg/kg) and then treated with acarbose (24 mg/kg) and Thymus vulgaris extract (0.4 ml/kg).[13]

After 14 days of this trial, the rats were euthanized with xylocaine (10 mg/kg) and ketamine (80 mg/kg).[14] Blood samples were collected from all rats that underwent laparotomy, and serum was prepared for chemical analysis. The kit was superoxide dismutase kit (SOD), C-peptide kit, advanced oxidation protein product kit (AOPP), and glucometer was used to measure blood glucose levels were used.

All analyses were performed using SPSS-26. Statistical evaluation was conducted using one-way analysis of variance (ANOVA) followed by Student's t-test where appropriate. A probability value of less than 0.05 was regarded as statistically significant.

RESULTS

The biochemical variables in groups are in Table 1. A statistically significant reduction in plasma SOD concentration was observed in the diabetic control group (Group B) when compared with both the negative control (Group A) and the combined treatment group (Group D). In contrast, the acarbose-treated group (Group C) did not demonstrate a statistically meaningful difference relative to Group B in Figure 1.

Table 2 shown the SOD levels in Group A were markedly higher than in Groups C and D ($p=0.001$). Additionally, Group D exhibited a significant improvement in SOD concentration compared with Group B ($p=0.035$). However, the difference between Groups C and B did not reach statistical significance ($p=0.098$). Statistical significance was defined at $p<0.05$

Plasma content of C-peptide: C-peptide levels were expressed as mean ± SD. The diabetic control group (Group B) showed a marked reduction compared with the negative control (Group A). Both treatment groups, acarbose (Group C) and acarbose plus thymol (Group D) in Figure 2, demonstrated significantly higher C-

peptide levels than Group B (p=0.002 and p=0.001, respectively). No significant differences were observed between Groups C or D and the negative control (p>0.05) [Table 3].

Table No. 1: Biochemical variables in the studied groups

Groups	SOD (pg/ml)	C- peptide (pg/ml)	AOPP (pg/ml)	Glucose (mg/dl)
A	1.093±0.64	1292.82±208.58	281.61±49.68	95.9 ± 18.69
B	0.337±0.091*	863.17±250.14*	430.37±77.85*	148±29.71*
C	0.554±0.155	1248.78±303.68*	271.42±120.38*	102.9±12.74*
D	0.615 ±0.202*	1368.33±277.35*	269.74±59.11*	97±7.46*

*p<0.05 (Significant)

Table No. 2: Comparison between the effects of treatment on superoxide dismutase level in studied groups

Variable	Group	Study groups	Mean±SD	P- value
Superoxide dismutase (pg/ml)	Group C (0.554±0.155)	Group A	1.093±0.64	0.001
		Group B	0.337±0.091	0.098
	Group D (0.615±0.202)	Group A	1.093±0.64	0.001
		Group B	0.337±0.091	0.035

P<0.05 (Significant)

Table No. 3: Comparison between the effect of treatment on C-peptide level in studied groups

Variable	Group	Study groups	Mean±SD	P- value
C-peptide (pg/ml)	Group C (1248.78±303.68)	Group A	1292.82±208.58	0.716
		Group B	863.17±250.14	0.002
	Group D (1368.33±277.35)	Group A	1292.82±208.58	0.534
		Group B	863.17±250.14	0.001

P<0.05 (Significant)

Table No. 4: Comparison between the effects of treatment on AOPP level in studied groups

Variable	Group	Study groups	Mean±SD	P- value
AOPP (pg/ml)	Group C (271.42±120.38)	Group A	281.61±49.68	0.763
		Group B	430.37±77.85	0.001
	Group D (269.74±59.11)	Group A	281.61±49.68	0.726
		Group B	430.37±77.85	0.001

P<0.05 (Significant)

Table No. 5: Comparison between the effects of treatment on Blood glucose level in studied groups

Variable	Group	Study groups	Mean±SD	P- value
Blood glucose (mg/dl)	Group C (102.9±12.74)	Group A	95.9±18.69	0.348
		Group B	148±29.71	0.001
	Group D (97±7.46)	Group A	95.9±18.69	0.887
		Group B	148±29.71	0.001

P<0.05 (Significant)

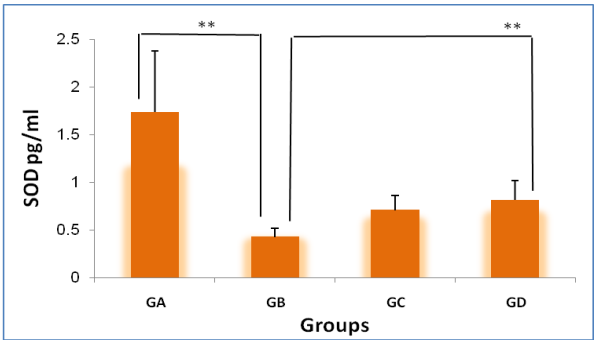

Figure No. 1: GA is controlled negative; GB is control positive (DM); GC is the treated group (Acarbose); GD is the treated group (Acarbose+Thymol), (p<0.05 compared to positive control)**

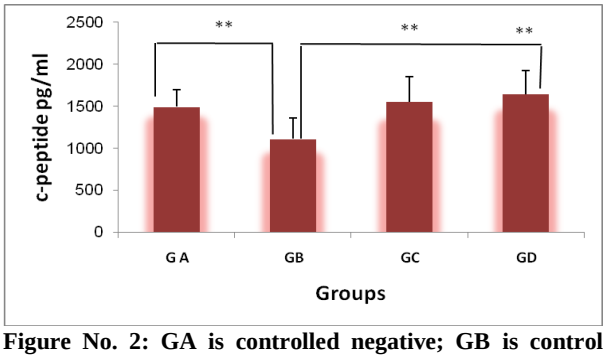

Figure No. 2: GA is controlled negative; GB is control positive (DM); GC is the treated group (Acarbose); GD is the treated group (Acarbose+Thymol), (p<0.05 compared to positive control)**

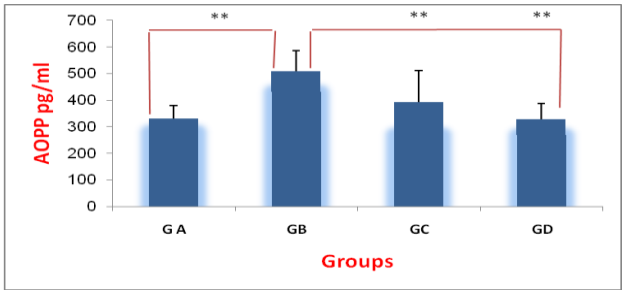

Figure No. 3: GA is controlled negative;GB is control positive (DM); GC is the treated group (Acarbose); GD is the treated group (Acarbose+Thymol), (p<0.05 compared to positive control)**

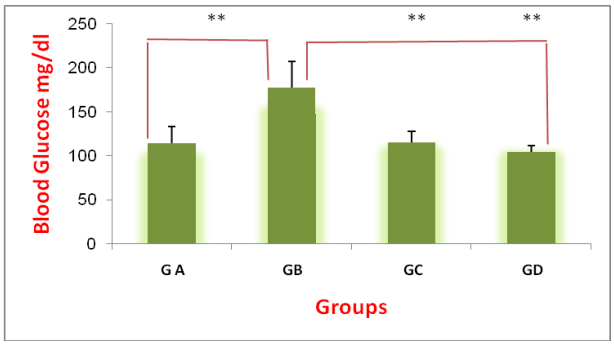

Figure No. 4: GA is controlled negative;GB is control positive (DM); GC is the treated group (Acarbose); GD is the treated group (Acarbose+Thymol), (p<0.05 compared to positive control)**

Plasma AOPP concentrations were markedly elevated in the diabetic control group (Group B) compared with the negative control (Group A). Both treatment groups, acarbose (Group C) and acarbose combined with thymol (Group D), showed a significant reduction in AOPP levels relative to Group B (p=0.001 for both comparisons). No statistically significant differences were detected between Groups C or D and the negative control (p>0.05). Statistical significance was defined at p<0.05 (Fig. 3, Table 4).

Blood glucose levels were significantly higher in the diabetic control group (Group B) than in the negative control group (Group A). Treatment with acarbose alone (Group C) or in combination with thymol (Group D) resulted in a significant decrease in glucose levels compared with Group B (p = 0.001). Neither treatment group differed significantly from the negative control (p>0.05). Statistical significance was set at p<0.05 (Fig. 4, Table 5).

DISCUSSION

The present study demonstrated that induction of diabetes by STZ produced clear metabolic and oxidative disturbances in rats, as evidenced by the significant elevation in blood glucose[15] and AOPP levels[16], and marked reduction in SOD[17] and C-peptide concentrations. These alterations reflected the well-established action of STZ, which are selective target pancreatic β-cell through DNA alkylation and over production of reactive oxygen species (ROS), leading to impaired insulin secretion and severe oxidative imbalance.[18]

Acarbose treatment (Group C) produced significant improvements in all measured biomarkers compared with the diabetic control (Group B). Blood glucose levels were significantly reduced, therefore, acarbose modulated oxidative stress[19] and enhance antioxidant stats.[20] These results are consistent with the known pharmacological actions of acarbose, which include the reduction of glucose absorption. The elevation of c-peptide suggests preserve β cell function.

Thymus vulgaris combined with acarbose (Group D), produced additional improvements in oxidative and glycemic parameters, consistently showing superior trends in increasing SOD activity, reducing AOPP levels, and improving glucose control. These enhancements likely reflect the potent antioxidant properties of thymol. As a phenolic monoterpene, thymol effectively neutralizes free radicals, stabilizes cellular membranes, prevents lipid and protein oxidation, and upregulates endogenous antioxidant enzymes.[21] Furthermore, thymol has been reported to improve glucose metabolism, reduce insulin resistance, and preserve pancreatic tissue integrity, which supports the improved C-peptide trends observed in this study.

The significant reduction in AOPP levels in the treatment groups highlights the efficacy of both acarbose and thymol in minimizing oxidative protein damage. AOPP is a well-established biomarker of oxidative stress and protein oxidation, and its levels are commonly elevated in diabetes due to persistent hyperglycemia and chronic inflammation.[22] The ability of the acarbose-thymol combination to reduce AOPP more effectively suggests enhanced antioxidant synergy, whereas thymol directly scavenges free radicals.

Similarly, the increase in SOD levels in combination therapy emphasizes the potential of thymol to stimulate endogenous antioxidant defenses. SOD is a critical enzyme that converts superoxide radicals into less harmful molecules. Its depletion in diabetic rats reflects increased oxidative burden, whereas its elevation following therapy indicates restoration of redox balance. The higher SOD activity in the acarbose + thymol group suggests a greater capacity to counteract oxidative injury than acarbose alone, although, the difference did not reach statistical significance.

Regarding glycemic control, all treatment groups showed substantial reductions in blood glucose levels compared to diabetic controls. However, the combination therapy group (D) demonstrated the most pronounced reduction. This improvement may be attributed not only to the pharmacological effects of acarbose on carbohydrate metabolism but also to

thymol's ability to modulate glucose uptake and enhance insulin receptor signaling.

The accompanying improvement in C-peptide levels further supports better β-cell performance or preservation under combination therapy.

CONCLUSION

The notable pancreatic protection effect in diabetes animal model, indicating the beneficial role of acarbose and thymol in reducing oxidative stress, restoring β-cell function, increasing antioxidant state, and improving glucose levels. Thymol enhances the antioxidant properties of acarbose. Therefore, Acarbose is effective in glycemic control and reducing oxidative stress. Combination with thymol shows additional therapeutic benefits.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Asma A. Alkafaji, Majid Kadhim Abbas
Drafting or Revising Critically:	Asma A. Alkafaji, Majid Kadhim Abbas
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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