

Antihyperglycemic and metabolic regulatory effects of *Artemisia vulgaris* L. in alloxan-induced diabetic female wistar rats

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ABSTRACT

Diabetes mellitus is one of the most prevalent endocrine disorders worldwide. Although insulin therapy, pharmacotherapy, and dietary management are commonly used to control the disease, medicinal plants are increasingly being explored for the management of diabetes and its associated complications. This study investigated the antihyperglycemic and metabolic regulatory effects of *Artemisia vulgaris* L. aqueous extract, with emphasis on its nutrient-enhancing properties, on glucose homeostasis and diabetes-associated metabolic dysfunction in alloxan-induced diabetic female Wistar rats. Forty-two female Wistar rats were randomly divided into six groups (n = 7): control, diabetic control, and diabetic groups treated with different doses of *A. vulgaris* extract. Diabetes was induced using a single intraperitoneal dose of alloxan monohydrate (150 mg/kg body weight). The extract was administered orally once daily for 30 days. At the end of the treatment period, fasting blood glucose (FBG), serum lipid profile (total cholesterol, triglycerides, HDL-C, and LDL-C), serum proteins (total protein and albumin), renal function markers (urea and creatinine), and liver enzyme activities (AST, ALT, and ALP) were determined. Percentage change in body weight was also calculated. Alloxan-induced diabetes significantly ($p < 0.05$) decreased body weight, HDL-C, total protein, and albumin, while increasing FBG, AST, ALT, ALP, urea, creatinine, total cholesterol, triglycerides, and LDL-C. Treatment with *A. vulgaris* extract significantly ameliorated these alterations in a dose-dependent manner. Body weight increased from 161.0 ± 0.5 – 201.9 ± 2.9 g after induction to 166.7 ± 0.9 – 259.7 ± 3.6 g following treatment, while FBG decreased from 4.09 ± 0.04 – 4.64 ± 0.06 mmol/L to 2.96 ± 0.07 – 3.68 ± 0.03 mmol/L. Renal and hepatic function markers, as well as lipid profile parameters, also improved across all treatment groups, with the 400 mg/kg dose producing effects comparable to the standard antidiabetic drug.

Keywords: *Artemisia vulgaris*, alloxan-induced diabetes, antihyperglycemic activity, metabolic regulation, female wistar rats.

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List of Abbreviation - TC = total cholesterol, TRIG = triglycerides, HDL = high-density lipoproteins, LDL = low-density lipoproteins, TP = total proteins, ALB = albumin, CR = creatinine, UR = urea, AST = aspartate transaminase, ALT = alanine transaminase, ALP = alkaline phosphatase, WHO = World Health Organization, IDF = International Diabetes Federation, AV = *Artemisia vulgaris*.

INTRODUCTION

Diabetes mellitus (DM) is a complex and rapidly growing global health problem affecting both developed and developing countries (Mishra et al., 2024). The World Health Organization (WHO) defines diabetes as a group

of metabolic disorders characterized by impaired metabolism of carbohydrates, fats, and proteins due to inadequate insulin secretion, reduced tissue sensitivity to insulin, or both (WHO, 2017). Current therapeutic options

include insulin and other agents such as amylin analogues, α -glucosidase inhibitors, sulphonylureas, and biguanides. However, these drugs are often associated with adverse effects, including hypoglycemia, hepatic dysfunction, lactic acidosis, and gastrointestinal disturbances (Khan, 2024).

In addition to conventional pharmacotherapy, medicinal plants such as *Artemisia vulgaris* have gained increasing attention as complementary or alternative strategies for diabetes management. Traditional herbal medicines remain integral to healthcare worldwide, particularly in resource-limited settings, because of their reported efficacy, lower incidence of side effects, and cost-effectiveness compared with synthetic antidiabetic drugs (Saggar et al., 2022). The International Diabetes Federation estimates that approximately 425 million people worldwide are living with diabetes, with nearly 50% remaining undiagnosed, highlighting its magnitude as a global public health concern (IDF, 2017). Diabetes mellitus is a major risk factor for debilitating complications, including blindness, cerebrovascular disease, renal failure, and limb amputations (Mohiuddin, 2019). Its rising prevalence is driven by rapid population growth, urbanization, population ageing, obesity, and physical inactivity (Almalki and Khan, 2025). In Nigeria, the burden is further compounded by weak healthcare systems, unhealthy diets, sedentary lifestyles, and poverty, which contribute to underdiagnosis and disease progression (Almalki and Khan, 2025).

In Western and African traditional medicine, several species of the genus *Artemisia* are widely used for their reputed therapeutic properties. More than 400 species have been reported to exhibit antidiabetic activity, and many *Artemisia* species are commonly employed in the traditional management of diabetes mellitus (Eshetu et al., 2016). *Artemisia vulgaris*, a member of the Asteraceae family, is a well-known medicinal plant used globally in the treatment of various ailments (Siwan et al., 2022). The genus *Artemisia* comprises over 400 species distributed worldwide (Sharma and Kandel, 2014). In Nigeria, although *Artemisia* species are largely imported, they occupy a broad ecological range and attract significant scientific and economic interest due to their notable medicinal properties and commercial value (Orege et al., 2023).

The health benefits of *A. vulgaris*, particularly its essential oil and plant extracts, have attracted considerable scientific attention. These extracts have been traditionally used for the treatment of several diseases, and substantial scientific evidence supports their antiepileptic, antihysterical, diuretic, digestive, and stimulant properties (Ben-Nasr et al., 2013). In folk medicine, the leaves and whole plant are used in the management of diabetes, epilepsy, psychoneurosis, depression, irritability, insomnia, anxiety, and stress (Ashok and Upadhyaya, 2013; Rai et al., 2012). Additionally, *A. vulgaris* exhibits antispasmodic, antiseptic, antibacterial, antimalarial, antitumor,

antirheumatic, and hepatoprotective activities (Gonfa et al., 2025).

The medicinal value of *A. vulgaris* has been attributed largely to its phytochemical constituents, particularly flavonoids, which are known for their strong antioxidant properties and associated health benefits (Karak, 2019). In this study, the effects of varying doses of *Artemisia vulgaris* on alloxan-induced hyperglycemia in female Wistar rats were investigated. It was hypothesized that daily administration of *A. vulgaris* for 30 days would significantly reduce fasting blood glucose levels in diabetic female Wistar rats.

MATERIALS AND METHODS

Plant collection

Fresh leaves of *Artemisia vulgaris* L. were collected from A-Z Biotechnology Limited Medicinal Plant Plantation. The plant was authenticated at the Herbarium Unit, Department of Plant Science, University of Jos, Nigeria, and assigned the voucher number: JUHN21000361.

Experimental animals and housing

Forty-two healthy female Wistar rats (180–260 g) were obtained from the Animal House, University of Jos. The animals were housed in clean plastic cages containing wood-chip bedding and provided with standard rodent pellets and water ad libitum. They were maintained under standard laboratory conditions of 25 ± 2 °C, $50 \pm 15\%$ relative humidity, and a 12-h light/dark cycle (Ghasemi et al., 2021). Baseline body weight, fasting blood glucose, lipid profile, renal function, and liver function indices were recorded before the experiment.

Induction of diabetes

Diabetes was induced using alloxan monohydrate according to Hauwa'u et al. (2014). A stock solution was prepared by dissolving 1.8 g of alloxan monohydrate in 12 mL of sterile distilled water to obtain a concentration of 150 mg/mL. After overnight fasting, rats received a single intraperitoneal injection of alloxan at 150 mg/kg body weight. Blood samples were collected to determine fasting blood glucose, lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C), renal function markers (creatinine and urea), and liver enzymes. Rats with fasting blood glucose ≥ 200 mg/dL were considered diabetic and included in the study.

Monitoring and data collection

Both control and diabetic rats were fasted for 12 h before

measurements, with free access to water. Body weight, fasting blood glucose, lipid profile, renal function, and liver indices were measured at baseline, after diabetes induction, and at the end of the experiment. Fasting blood glucose was determined weekly for four weeks using a digital glucometer (Accu-Chek®) from tail-vein blood, while other biochemical parameters were analyzed using a Cobas c111 analyzer.

Experimental design

The experimental protocol was approved by the institutional ethical committee (Approval No.: F17-00379). Rats were divided into six groups (n = 7):

- Group I: Normal control (non-diabetic, untreated)
- Group II: Diabetic control (untreated)
- Group III: Diabetic + standard drug (glibenclamide, 5 mg/kg)
- Group IV: Diabetic + *A. vulgaris* extract (100 mg/kg)
- Group V: Diabetic + *A. vulgaris* extract (200 mg/kg)
- Group VI: Diabetic + *A. vulgaris* extract (400 mg/kg)

Treatments were administered orally once daily for 30 days.

Statistical analysis

Data were analyzed using GraphPad Prism (version 8.0). One-way analysis of variance (ANOVA) was used to determine significant differences among groups. Results are expressed as mean \pm standard deviation (SD).

Statistical significance was accepted at $p < 0.05$.

RESULTS

Effect of *A. vulgaris* extract on body weight

Diabetes induction caused a significant reduction in body weight across all experimental groups (Figure 1). In the *Artemisia* treated groups, baseline body weights ranged from 161.0 ± 0.5 to 201.9 ± 2.9 g and decreased following alloxan administration. After treatment, body weight increased progressively in all treated groups. Final body weights were 166.7 ± 0.9 g, 225.1 ± 3.0 g, and 259.7 ± 3.6 g for the 100, 200, and 400 mg/kg extract groups, respectively, while the standard drug group reached 197.9 ± 1.8 g, indicating recovery from diabetes-induced weight loss.

Effect on fasting blood glucose

Fasting blood glucose (FBG) increased markedly after diabetes induction in all groups. Baseline FBG values ranged from 4.09 ± 0.04 to 4.64 ± 0.06 mmol/L in the extract-treated groups and 5.0 ± 0.3 mmol/L in the standard drug group. Following treatment, FBG decreased significantly, reaching 3.68 ± 0.03 , 2.96 ± 0.07 , and 3.07 ± 0.06 mmol/L for the 100, 200, and 400 mg/kg extract groups, respectively, while the standard drug group declined to 3.4 ± 0.3 mmol/L (Figure 2). These results indicate effective glycemic control by *A. vulgaris*, particularly at 200 and 400 mg/kg.

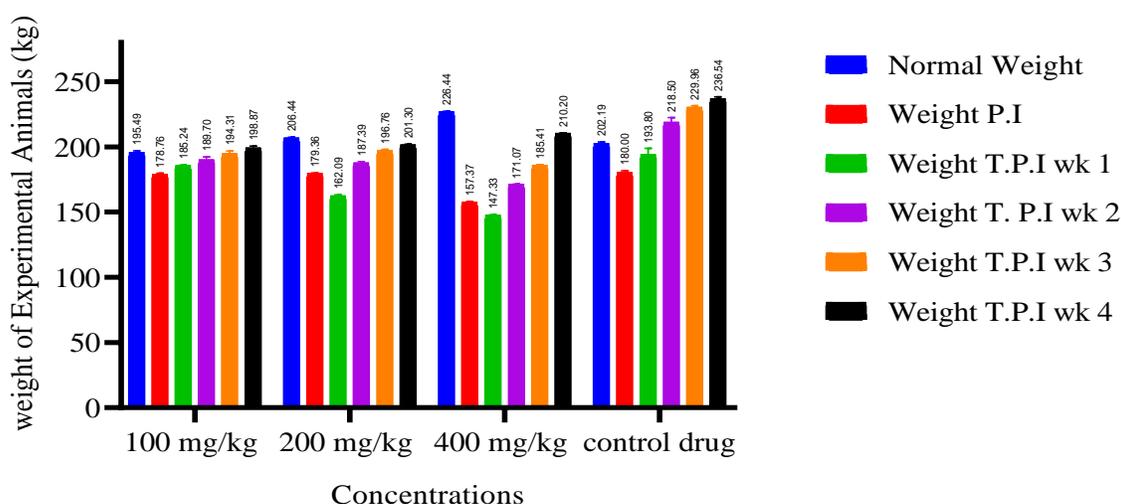


Figure 1. Effects of aqueous leaf extract of *A. vulgaris* on the body weight of alloxan-induced diabetic rats.

Weight P.I= Body weight of rats post alloxan-induction

Weight T.P.I= Body weight of rats one week after treatment post alloxan-induction

Weight T.P.I= Body weight of rats two weeks after treatment post alloxan-induction

Weight T.P.I= Body weight of rats three weeks after treatment post alloxan-induction

Weight T.P.I= Body weight of rats four weeks after treatment post alloxan-induction.

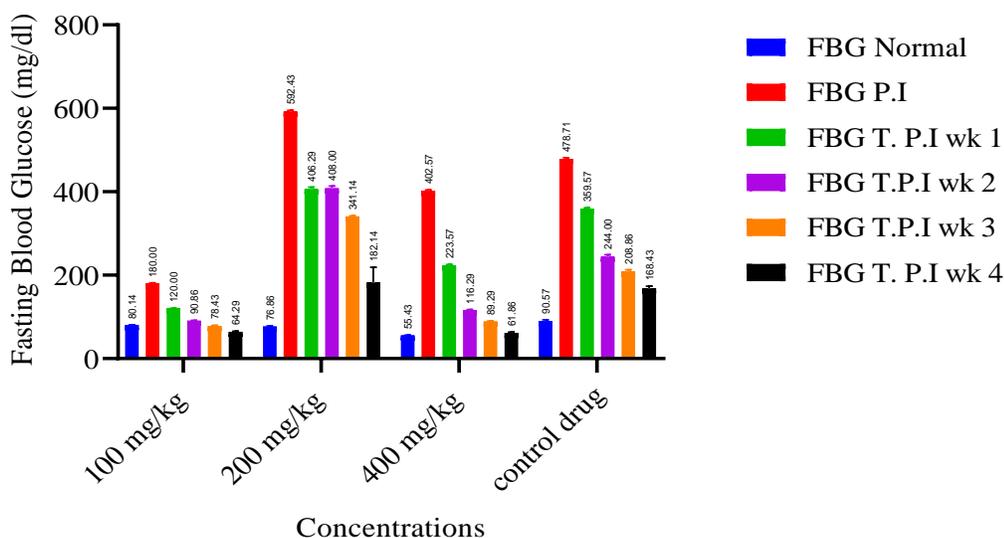


Figure 2. Effects of aqueous leaf extract of *A. vulgaris* on the blood glucose of alloxan-induced diabetic rats.

FBG P.I.= Fasting blood glucose of rats post alloxan-induction
 FBG T.P.I.= Fasting blood glucose of rats one week after treatment post alloxan-induction
 FBG T.P.I.= Fasting blood glucose of rats two weeks after treatment post alloxan-induction
 FBG T.P.I.= Fasting blood glucose of rats three weeks after treatment post alloxan-induction
 FBG T.P.I.= Fasting blood glucose of rats four weeks after treatment post alloxan-induction.

Effect on renal function

Alloxan-induced diabetic rats showed significantly elevated creatinine (1.43 ± 0.05 mg/L) and urea (30.69 ± 0.49 mmol/L) compared with the control group (0.49 ± 0.04 mg/L and 5.80 ± 0.01 mmol/L, respectively). Treatment with *A. vulgaris* significantly reduced these values in a dose-dependent manner (Table 1), indicating improvement in renal function.

Effect on lipid profile

Significant differences ($p < 0.05$) were observed in lipid parameters across groups (Table 2). Diabetes increased total cholesterol and triglycerides and reduced HDL-C. Treatment with *A. vulgaris*, particularly at 400 mg/kg, significantly lowered total cholesterol and triglycerides and improved HDL-C, indicating antihyperlipidemic activity.

Table 1. Effects of aqueous leaf extract of *A. vulgaris* on renal function tests in alloxan-induced diabetic rats.

Groups	Creatinine (CR, mg/L)	Urea (UR, mmol/L)
Control	0.49 ± 0.04^b	5.80 ± 0.01^c
Alloxan	1.43 ± 0.05^a	30.69 ± 0.49^a
Alloxan + STD	0.57 ± 0.05^b	10.81 ± 0.01^b
Alloxan + A.v100	0.40 ± 0.00^b	6.02 ± 0.01^b
Alloxan + A.v200	0.57 ± 0.05^b	10.81 ± 0.01^b
Alloxan + A.v400	0.54 ± 0.05^b	13.31 ± 0.01^b
L.S.D	0.18	
S.F	****	

Each value represents Mean \pm S.E. (n=7 rats). Values with different superscripts differ significantly ($P < 0.01$). **CR** = Creatinine, **UR** = Urea.

Effect on liver function

Diabetic rats exhibited marked alterations in liver

enzymes and serum proteins, including increased AST and ALP and reduced total protein and albumin. Treatment with *A. vulgaris* improved these biochemical

Table 2. Antidiabetic effects of aqueous leaf extract of *A. vulgaris* on lipid profile in female diabetic rats.

Groups	TCHO, (mmol/L)	LDL (mg/L)	HDL (mg/L)	TRIG (mg/L)
Control	1.29 ± 0.01 ^b	0.07 ± 0.01 ^a	1.02 ± 0.00 ^a	0.45 ± 0.01 ^c
DMBA	1.44 ± 0.01 ^a	-0.01 ± 0.01 ^c	0.98 ± 0.00 ^b	1.04 ± 0.01 ^a
DMBA + STD	2.13 ± 0.01 ^c	0.76 ± 0.01 ^a	0.92 ± 0.01 ^b	0.98 ± 0.01 ^b
DMBA + A.v100	1.17 ± 0.00 ^c	0.08 ± 0.01 ^b	0.82 ± 0.01 ^b	0.61 ± 0.01 ^b
DMBA + A.v200	1.83 ± 0.01 ^b	0.75 ± 0.00 ^b	0.73 ± 0.00 ^b	0.76 ± 0.01 ^b
DMBA + A.v400	0.71 ± 0.01 ^c	-0.21 ± 0.01 ^b	0.78 ± 0.01 ^c	0.29 ± 0.00 ^c
L.S.D	0.006			
S.F	****			

Values in the same row with the same superscript letters do not differ significantly. **L.S.D** = Least Significant Different; **S.F** = Significant Figure; Each value represents Mean ± SE.

TCHO = Total Cholesterol, **LDL** = Low Density lipoprotein, **HDL** = High Density lipoprotein, **TRIG** = Triglycerides.

Table 3. Effects of aqueous leaf extracts of *A. vulgaris* on liver function level in alloxan-induced diabetic rats.

Groups	AST (u/L)	ALT (u/L)	ALP (u/L)	TP(g/L)	ALB,(g/L)	TB(g/L)
Control	33.60 ± 0.06 ^c	99.31 ± 0.07 ^a	361.21 ± 0.44 ^c	7.21 ± 0.07 ^a	44.92 ± 0.05 ^a	2.51 ± 0.11 ^b
DMBA	210.33 ± 0.53 ^a	72.61 ± 0.41 ^b	461.24 ± 0.44 ^b	6.73 ± 0.05 ^b	33.32 ± 0.01 ^b	2.73 ± 0.05 ^a
DMBA + STD	158.34 ± 0.32 ^b	66.51 ± 0.62 ^c	305.63 ± 0.35 ^b	6.57 ± 0.08 ^b	38.85 ± 0.52 ^b	1.23 ± 0.05 ^c
DMBA + A.v100	147.10 ± 0.08 ^b	108.74 ± 0.37 ^a	455.02 ± 0.05 ^a	5.90 ± 0.00 ^b	35.11 ± 0.01 ^c	1.71 ± 0.04 ^b
DMBA + A.v200	381.19 ± 0.74 ^a	235.36 ± 0.59 ^a	276.19 ± 0.43 ^a	6.44 ± 0.05 ^b	36.37 ± 0.01 ^c	1.20 ± 0.00 ^c
DMBA + A.v400	246.90 ± 0.28 ^b	56.84 ± 0.39 ^c	601.80 ± 0.54 ^a	5.27 ± 0.05 ^c	18.76 ± 0.01 ^c	2.10 ± 0.00 ^b
L.S.D	0.50					
S.F	****					

Values in the same row with the same superscript letters do not differ significantly. **L.S.D** = Least Significant Different; **S.F** = Significant Figure; Each value represents Mean ± SE.

AST = Aspartate Transaminase, **ALT** = Alkaline Transaminase, **ALP** = Alanine Phosphatase, **TP** = Total Protein, **ALB** = Albumin, **TB** = Total Bilirubin.

indices (Table 3), suggesting hepatoprotective effects.

DISCUSSION

Administration of *Artemisia vulgaris* significantly modulated body weight in alloxan-induced diabetic rats. Untreated diabetic rats showed marked body-weight loss, which is commonly associated with increased glucose utilization and enhanced catabolism of lipids and proteins despite increased food intake (Kitada et al., 2018). In contrast, diabetic rats treated with *A. vulgaris* exhibited a dose-dependent restoration of body weight over 30 days, with values comparable to those of the standard drug-treated group and significantly higher than those of the untreated diabetic group. This finding is consistent with reports by Helal et al. (2014) and Ogbonna et al. (2017), who observed recovery of body weight in diabetic animals following treatment with *Artemisia annua*. Similarly, Daradka et al. (2014) demonstrated that *A. absinthium* significantly prevented weight loss in diabetic rats. The recovery of body weight observed in the present study may be attributed to improved glucose utilization as a result of enhanced insulin action, which reduces reliance on fat and protein catabolism for energy (Miteu,

2021).

Alloxan induces diabetes by selectively destroying pancreatic β -cells, leading to impaired insulin secretion and persistent hyperglycaemia (Longkumer et al., 2021). This insulin deficiency produces profound metabolic disturbances, including hyperglycaemia, dyslipidaemia, and hepatic and renal dysfunctions (Daradka et al., 2014). In the present study, alloxan-treated rats exhibited significantly elevated fasting blood glucose levels compared with normal controls. However, administration of *A. vulgaris* for 30 days produced a significant reduction in blood glucose in a dose-dependent manner. The reduction in blood glucose levels in diabetic rats was attributed to the hyposecretion of insulin by pancreatic β -cells. Alloxan selectively destroys β -cells and induces hyperglycemia (Queiroz et al., 2021). These results are consistent with earlier reports by Helal et al. (2014) and Eteng et al. (2013), who observed significant reductions in glucose levels following treatment with *Artemisia* extracts. The antihyperglycaemic effect may result from stimulation of insulin secretion by pancreatic β -cells, inhibition of α -cell activity, or enhancement of insulin sensitivity and peripheral glucose utilization (Ogbonna et al., 2017).

The glucose-lowering effect of *A. vulgaris* is likely

mediated by its bioactive phytochemicals, including flavonoids and artemisinin-related compounds. These constituents may enhance insulin secretion, improve insulin receptor sensitivity, or stimulate glucose-metabolizing enzymes, thereby restoring normoglycaemia. In addition, flavonoids possess antioxidant properties that may protect pancreatic β -cells from oxidative damage, further contributing to improved insulin production.

Betatrophin, a hormone secreted by the liver and adipose tissue, has been shown to stimulate pancreatic β -cell proliferation and insulin production (Yi et al., 2013). Improved liver function may increase betatrophin secretion, thereby enhancing insulin synthesis and promoting weight gain in diabetic animals (Helal et al., 2014). This mechanism may partly explain the improved glycaemic control and body-weight recovery observed in *A. vulgaris* treated rats.

Renal dysfunction is a common complication of diabetes and is often reflected by elevated serum urea and creatinine levels. In this study, untreated diabetic rats showed significantly increased urea and creatinine levels, indicating impaired renal function. These changes are likely due to metabolic disturbances associated with diabetes, including oxidative stress, lipid peroxidation, and altered protein and nucleic acid metabolism (Thongnak et al., 2020; Giribabu et al., 2017). Treatment with *A. vulgaris* significantly reduced serum urea and creatinine levels in a dose-dependent manner, restoring them toward normal values. This suggests that the extract mitigates diabetes-induced renal damage, possibly through improved glycaemic control and reduced oxidative stress. Similar nephroprotective effects of *Artemisia* species have been reported by Helal et al. (2014) and Daradka et al. (2014), as well as in systematic reviews of medicinal plant therapies for diabetic nephropathy (Veisi et al., 2022).

Dyslipidaemia is a major metabolic abnormality in diabetes and contributes significantly to cardiovascular risk. In the present study, diabetic rats showed elevated levels of total cholesterol, LDL, and triglycerides, consistent with previous reports (Ye et al., 2019). Treatment with *A. vulgaris* significantly reduced total cholesterol and LDL levels while increasing HDL, indicating a protective hypolipidaemic effect. These changes may be mediated by improved insulin activity, which suppresses lipolysis and reduces the influx of free fatty acids into the liver, thereby lowering hepatic lipid synthesis (Ježek et al., 2018). The lipid-modulating effects observed in this study agree with earlier findings by Khan (2015), who demonstrated that *A. vulgaris* root extract normalized serum lipid profiles in hyperlipidaemic rats.

Liver enzymes such as AST, ALT, and ALP are sensitive indicators of hepatocellular injury. In diabetic rats, significant elevations in these enzymes reflect liver damage resulting from insulin deficiency and excess free-fatty-acid accumulation (Bilal et al., 2016; Tamber et al.,

2023). Treatment with *A. vulgaris* reduced the activities of these enzymes, indicating hepatoprotective effects. Furthermore, diabetes-induced reductions in total protein, albumin, and bilirubin were partially reversed by the extract. Insulin plays a key role in protein synthesis and metabolism; thus, hypoinsulinaemia in diabetes contributes to protein depletion (Abdulla et al., 2016). The restoration of these parameters suggests that *A. vulgaris* improves hepatic synthetic function, possibly through enhanced insulin action and antioxidant protection afforded by its flavonoid content (Fatma et al., 2013; Ram et al., 2014; Ghanbari et al., 2016).

CONCLUSION

The present study demonstrates that *Artemisia vulgaris* aqueous leaf extract exerts significant antihyperglycaemic effects in alloxan-induced diabetic rats, accompanied by prevention of body-weight loss and improvement in diabetes-associated alterations in renal, hepatic, and lipid parameters. These findings indicate that *A. vulgaris* possesses protective and regulatory effects against metabolic dysfunctions associated with diabetes. Further phytochemical characterization and mechanistic studies are required to identify the active compounds and validate its therapeutic potential for diabetes management.

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