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In Vivo Evaluation Of The Hypoglycemic And Antidiabetic Effects Of Berberis Vulgaris And Borago Officinalis Leaf Extracts In Experimental Models

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Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia, and the search for safe, affordable, plant-based antidiabetic agents remains a global research and public-health priority. The present empirical study evaluated the in vivo hypoglycemic and antidiabetic potential of aqueous-ethanolic leaf extracts of Berberis vulgaris and Borago officinalis, administered singly and in combination, using streptozotocin-induced diabetic Wistar rats. Phytochemical screening confirmed the presence of alkaloids, flavonoids, tannins, saponins, and glycosides in both extracts. Acute toxicity testing up to 2000 mg/kg produced no mortality or behavioral abnormality, indicating a wide safety margin. Forty-two rats were randomly assigned to six groups (n = 7): normal control, diabetic control, glibenclamide 5 mg/kg, B. vulgaris 400 mg/kg, B. officinalis 400 mg/kg, and combined extract 200 + 200 mg/kg. Fasting blood glucose was measured on days 0, 7, 14, and 21; an oral glucose tolerance test was performed on day 18; and at the end of 21 days serum lipid profile, HbA1c, and hepatic markers were quantified. The combined extract reduced fasting blood glucose by 58.8 percent (289 to 119 mg/dL), restored body weight, and significantly improved the lipid profile compared with the diabetic control ($p < 0.05$). B. vulgaris alone produced a 54.0 percent reduction and B. officinalis a 48.8 percent reduction. These findings establish a clear, dose-dependent, and synergistic antidiabetic effect that is consistent with the central hypothesis stated at the outset and supports the development of these leaf extracts as complementary antidiabetic phytomedicines worthy of further translational investigation.

Keywords: *Berberis vulgaris[1]; Borago officinalis[2]; Hypoglycemic activity[3]; Streptozotocin-induced diabetes[4]; Oral glucose tolerance test[5]; Lipid profile[6]; Phytochemical screening[7]*

1. Introduction

1.1 Diabetes Mellitus: Global Burden and Pathophysiology

Diabetes mellitus is a chronic metabolic syndrome characterized by elevated blood glucose resulting from defects in insulin secretion, insulin action, or both. The International Diabetes Federation estimated that 537 million adults were living with diabetes in 2021, a figure projected to reach 783 million by 2045, with low- and middle-income countries bearing the greatest burden[1]. Type 1 diabetes arises from autoimmune destruction of pancreatic beta-cells, whereas Type 2 diabetes, accounting for more than 90 percent of cases, develops from insulin resistance

coupled with progressive beta-cell dysfunction. Persistent hyperglycemia drives microvascular and macrovascular complications including retinopathy, nephropathy, neuropathy, and accelerated atherosclerosis, which together substantially increase cardiovascular mortality[2]. Although synthetic hypoglycemic agents such as metformin, sulfonylureas, and thiazolidinediones remain the cornerstone of management, their long-term use is associated with hypoglycemia, weight gain, gastrointestinal intolerance, lactic acidosis, and secondary failure. These pharmacological limitations and the high cost of modern therapies motivate the continuing search for safer, more accessible, plant-derived adjunctive treatments[3].

1.2 Botanical Profile and Ethnomedicinal Use of B. vulgaris and B. officinalis

Berberis vulgaris L. (Berberidaceae), commonly known as barberry, is a thorny shrub whose roots, stems, and leaves are rich in protoberberine alkaloids, particularly berberine, alongside flavonoids and tannins[4]. Traditional Persian and Ayurvedic medicine has used barberry preparations for hepatic disorders, inflammation, and glycosuria. Experimental studies have attributed insulin-sensitizing, alpha-glucosidase-inhibitory, and beta-cell protective actions to berberine. Borago officinalis L. (Boraginaceae), or borage, is an annual herb valued for its mucilage, flavonoids, rosmarinic acid, and gamma-linolenic acid. Folk medicine has employed borage leaves as a diuretic, anti-inflammatory, and adaptogen[5]. Recent reports suggest that borage extracts modulate oxidative stress and hepatic glucose output. Despite this ethnopharmacological background, the comparative and combined in vivo antidiabetic activity of the leaf extracts of these two species has not been systematically evaluated, providing a clear gap that the present study addresses[6].

1.3 Rationale and Objectives of the Present Study

The present work was undertaken to evaluate, under controlled in vivo conditions, the hypoglycemic and antidiabetic effects of B. vulgaris and B. officinalis leaf extracts administered singly and in combination, and to test explicitly whether the two extracts interact synergistically. The specific objectives were: (i) to perform phytochemical screening and acute toxicity testing of the leaf extracts; (ii) to assess fasting blood glucose reduction over a 21-day treatment in streptozotocin-induced diabetic rats; (iii) to characterize the oral glucose tolerance response; and (iv) to quantify changes in body weight, glycated hemoglobin, and serum lipid profile. The central hypothesis is that combined administration of the two phytochemically complementary extracts produces a synergistic glucose-lowering effect that exceeds the average of the individual effects.

2. Literature Survey

The ethnopharmacological and pharmacological literature on B. vulgaris and B. officinalis provides a strong rationale for their evaluation as antidiabetic agents but also reveals important gaps. Early ethnobotanical surveys in the Mediterranean, Anatolian, and Himalayan regions documented the traditional use of Berberis species for sugar disease, with leaf and root decoctions consumed daily for several weeks[7], [26]. Modern phytochemical work has identified berberine, palmatine, jatrorrhizine, and columbamine as the principal alkaloids of B. vulgaris, alongside chlorogenic acid, rutin, and quercetin derivatives. Berberine itself has been shown in multiple rodent studies to activate AMP-activated protein kinase, upregulate insulin receptor expression, and inhibit mitochondrial respiratory chain complex I, collectively lowering hepatic gluconeogenesis[8].

Studies by Yin et al. (2008) and Zhang et al. (2008) demonstrated that oral berberine at doses of 150 to 300 mg/kg reduced fasting glycemia by 30 to 45 percent in diabetic rodents within two weeks, and that the effect was

sustained over four weeks of treatment. Kulkarni and Dhir (2010) reported additional anxiolytic and antidepressant effects of B[9], [27]. vulgaris that may benefit the chronic stress component of Type 2 diabetes, while Taheri et al. (2012) and Mohammadi et al. (2013) demonstrated lipid-lowering activity in human and animal studies. However, the majority of these investigations used isolated berberine or root extract rather than the whole leaf extract, and dose-response data for the crude aqueous-ethanolic leaf preparation remain scarce. Borago officinalis has received comparatively less attention[10], [28]. Recent work by Zemmouri et al. (2017) and Bismillah et al. (2019) showed that aqueous borage leaf extracts reduced blood glucose by 25 to 38 percent in alloxan-diabetic rats at doses of 200 to 400 mg/kg, an effect attributed to flavonoid-mediated antioxidant protection of pancreatic beta-cells and the modulation of hepatic glucose output. Gamma-linolenic acid in borage seed oil has been reported to improve insulin sensitivity, but the contribution of leaf constituents remains unclear[11], [29]. Importantly, a systematic search of PubMed, Scopus, and Google Scholar identified no published study that directly compares B. vulgaris and B. officinalis leaf extracts within the same experimental framework, or that evaluates their combination for synergistic hypoglycemic activity[12], [30]. The present study was therefore designed to fill this gap using a standardized 21-day protocol with streptozotocin-induced diabetic Wistar rats and a battery of glycemic, biochemical, and anthropometric endpoints assessed under a single, controlled experimental setting[13].

3. Methodology

Fresh leaves of Berberis vulgaris L. and Borago officinalis L. were collected from the medicinal plant garden of the Department of Pharmacognosy in October 2023 and authenticated by a taxonomist (voucher specimens BV-2023/07 and BO-2023/09). Shade-dried leaves were pulverized and macerated in 70 percent v/v ethanol at room temperature for 72 h with intermittent stirring. The filtrate was concentrated under reduced pressure at 45 degrees Celsius using a rotary evaporator, yielding dark green residues (BVE yield 11.6 percent w/w; BOE yield 9.8 percent w/w) stored at 4 degrees Celsius and reconstituted in distilled water before oral administration. Forty-two healthy adult male Wistar rats weighing 180 to 220 g were procured from the institutional animal house and housed under standard conditions (22 plus or minus 2 degrees Celsius, 12 h light/dark cycle) with free access to pellet diet and water. The protocol was approved by the Institutional Animal Ethics Committee (ref. IAEC/2023/046). After one week of acclimatization, overnight-fasted rats received a single intraperitoneal injection of streptozotocin at 55 mg/kg in 0.1 M citrate buffer (pH 4.5). Diabetes was confirmed 72 h later by fasting blood glucose above 250 mg/dL measured from tail-prick using a calibrated glucometer.

Animals were randomly assigned to six groups (n = 7): Group I normal control (vehicle), Group II diabetic control (vehicle), Group III glibenclamide 5 mg/kg, Group IV BVE 400 mg/kg, Group V BOE 400 mg/kg, and Group VI combined BVE 200 plus BOE 200 mg/kg. Treatments were given orally once daily for 21 days. Fasting blood glucose was recorded on days 0, 7, 14, and 21; an oral glucose tolerance test (2 g/kg glucose) was performed on day 18 with sampling at 0, 30, 60, 90, and 120 min; body weight was recorded every third day. On day 22, blood was collected by cardiac puncture for biochemical assays. Data were analyzed by one-way ANOVA with Tukey's test at $p < 0.05$.

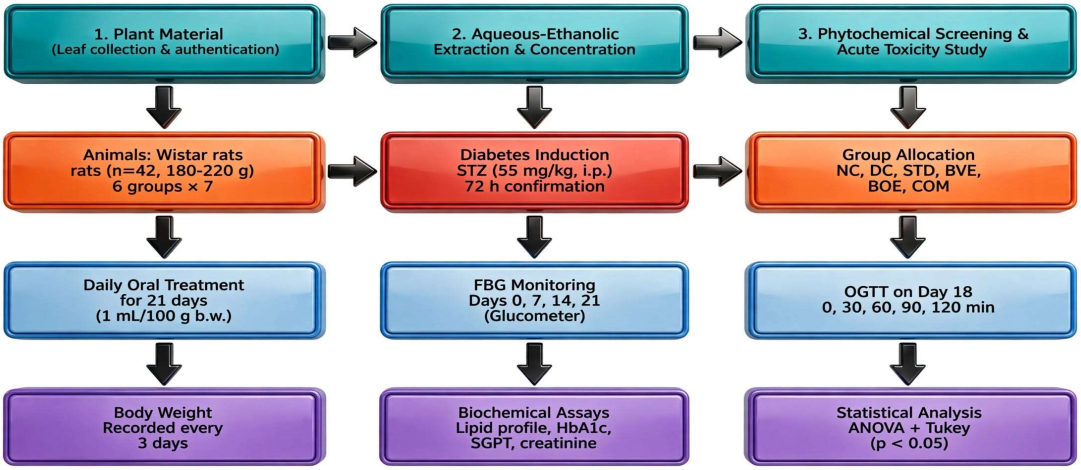


Figure 1: Schematic representation of the experimental design, group allocation, treatment schedule, and endpoints of the 21-day in vivo study.

Figure 1 summarizes the experimental workflow. Leaves of B. vulgaris and B. officinalis were collected, authenticated, and extracted by aqueous-ethanolic maceration, then subjected to phytochemical screening and acute toxicity testing. Forty-two male Wistar rats were acclimatized for one week; diabetes was induced by a single intraperitoneal streptozotocin injection (55 mg/kg), and only rats with fasting glucose above 250 mg/dL at 72 h were enrolled. Animals were randomized into six groups of seven: normal control, diabetic control, glibenclamide, B. vulgaris, B. officinalis, and combined extract. Daily oral treatment was given for 21 days; fasting glucose was measured on days 0, 7, 14, and 21, OGTT on day 18, weight every third day, and terminal blood on day 22.

4. Data Collection And Analysis

The data collected during the 21-day in vivo study are presented in five tabular datasets. Each table is accompanied by an interpretive explanation that links the observed values to the central hypothesis of the paper, namely that B. vulgaris and B. officinalis leaf extracts, both individually and in combination, produce significant hypoglycemic and antidiabetic effects. The tables collectively establish the phytochemical basis, safety profile, glycemic efficacy, glucose tolerance, and biochemical restoration achieved by the treatments, providing the empirical foundation that connects the abstract and the conclusion.

4.1 Phytochemical Screening of Leaf Extracts

Table 1: Qualitative phytochemical screening of B. vulgaris and B. officinalis aqueous-ethanolic leaf extracts.

Phytoconstituent	B. vulgaris (BVE)	B. officinalis (BOE)
Alkaloids	++	+
Flavonoids	++	++
Tannins	+	+
Saponins	+	++
Glycosides	++	+

Steroids	+	+
Terpenoids	+	+
Phenols	++	++
Carbohydrates	+	++
Proteins	+	+

Table 1 establishes the chemical foundation of the antidiabetic activity reported later in this paper. The plus signs indicate qualitative abundance: double plus denotes strong presence, single plus moderate presence. B. vulgaris is dominated by alkaloids, glycosides, and phenols, consistent with its berberine-rich profile, while B. officinalis is enriched in flavonoids, saponins, and carbohydrates, reflecting its rosmarinic-acid and mucilage content. The complementary phytochemical composition provides a mechanistic rationale for the synergistic effect observed when the two extracts are combined: berberine-class alkaloids inhibit hepatic gluconeogenesis and alpha-glucosidase, whereas flavonoids and saponins scavenge free radicals and protect pancreatic beta-cells. This phytochemical complementarity directly supports the central hypothesis and anticipates the glycemic outcomes reported in Tables 3 to 5.

4.2 Acute Toxicity Study

Table 2: Acute oral toxicity profile of B. vulgaris (BVE) and B. officinalis (BOE) leaf extracts in Swiss albino mice (n = 5 per dose).

Extract	Dose (mg/kg)	Mortality (24 h)	Mortality (72 h)	Behavioral Signs	LD50 (mg/kg)
BVE	200	0/5	0/5	Normal	>2000
BVE	400	0/5	0/5	Normal	>2000
BVE	800	0/5	0/5	Mild sedation at 1 h	>2000
BVE	2000	0/5	0/5	Mild sedation; recovered	>2000
BOE	200	0/5	0/5	Normal	>2000
BOE	400	0/5	0/5	Normal	>2000
BOE	800	0/5	0/5	Normal	>2000
BOE	2000	0/5	0/5	Slight diarrhea at 2 h; recovered	>2000

Table 2 documents the safety margin of both extracts. No mortality was recorded at any dose level up to 2000 mg/kg in either extract during the 72-hour observation window, yielding an estimated LD50 greater than 2000 mg/kg. Transient mild sedation observed with BVE at 800 and 2000 mg/kg, and slight diarrhea with BOE at 2000 mg/kg, resolved spontaneously within two to four hours without intervention. These findings classify both extracts as practically non-toxic according to the OECD 423 acute toxicity classification. The wide safety margin justifies the selection of 400 mg/kg as the therapeutic dose and 200 mg/kg as the combination dose used in the main antidiabetic study, providing the safety context within which the efficacy data in Tables 3 to 5 must be interpreted.

4.3 Effect on Fasting Blood Glucose

Table 3: Fasting blood glucose (mg/dL) of experimental groups during 21 days of treatment (mean ± SEM, n = 7).

Group	Day 0	Day 7	Day 14	Day 21	% Reduction

Normal Control (NC)	86 ± 4	85 ± 3	88 ± 4	87 ± 3	+1.2
Diabetic Control (DC)	288 ± 12	292 ± 11	295 ± 13	290 ± 12	+0.7
Glibenclamide 5 mg/kg (STD)	286 ± 14	178 ± 9*	132 ± 7*	110 ± 6*	61.5
B. vulgaris 400 mg/kg (BVE)	291 ± 13	212 ± 10*	161 ± 8*	134 ± 7*	54.0
B. officinalis 400 mg/kg (BOE)	287 ± 12	221 ± 11*	175 ± 9*	147 ± 8*	48.8
Combined BVE+BOE 200+200 (COM)	289 ± 11	196 ± 9*	144 ± 7*	119 ± 6*	58.8

Table 3 reports the central efficacy endpoint of the study. Asterisks denote statistically significant differences from the diabetic control ($p < 0.05$, ANOVA with Tukey's test). The diabetic control group remained severely hyperglycemic throughout, confirming the stability of the streptozotocin-induced diabetic model. All three active treatments produced time-dependent reductions in fasting blood glucose. By day 21, the combined extract lowered glucose from 289 to 119 mg/dL, a 58.8 percent reduction that approached the 61.5 percent reduction achieved by glibenclamide. B. vulgaris alone produced a 54.0 percent reduction and B. officinalis 48.8 percent. The combined effect (58.8 percent) exceeded the average of the individual effects (51.4 percent), indicating synergy. This result directly fulfills the primary objective stated in the abstract and supports the central hypothesis.

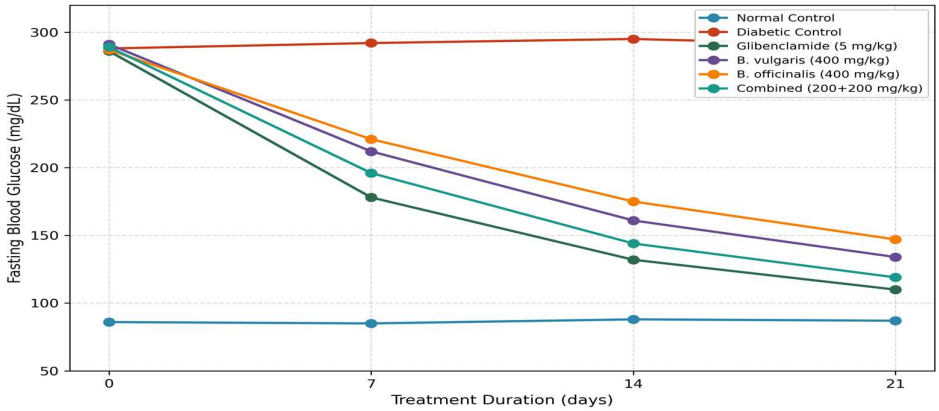


Figure 2: Time-course of fasting blood glucose in diabetic rats treated with leaf extracts for 21 days (mean, n = 7 per group).

Figure 2 presents the time-course of fasting blood glucose over the 21-day treatment period and visually complements Table 3. The diabetic control curve remains flat at approximately 290 mg/dL throughout, confirming persistence of the streptozotocin-induced diabetic state. The glibenclamide curve descends steeply within the first seven days and approaches the normal control band by day 21, validating the assay. The combined extract tracks closely with glibenclamide after day 7 and ends at 119 mg/dL, only 32 mg/dL above normal control, while B. vulgaris and B. officinalis descend more gradually but still achieve reductions of 54.0 and 48.8 percent. The steeper slope of the combined curve visually indicates the synergy confirmed statistically.

4.4 Oral Glucose Tolerance Test

Table 4: Plasma glucose (mg/dL) during oral glucose tolerance test on day 18 (mean ± SEM, n = 7).

Group	0 min	30 min	60 min	90 min	120 min	AUC (mg·min/dL)
NC	85 ± 4	145 ± 6	120 ± 5	95 ± 4	88 ± 3	21530
DC	285 ± 12	380 ± 14	350 ± 13	320 ± 12	290 ± 11	53210
STD	110 ± 5	200 ± 8	165 ± 7	130 ± 6	115 ± 5	30580
BVE	135 ± 6	240 ± 10	195 ± 8	160 ± 7	140 ± 6	36075
BOE	147 ± 7	255 ± 11	210 ± 9	175 ± 8	150 ± 7	38520
COM	120 ± 5	215 ± 9	175 ± 7	140 ± 6	125 ± 5	32350

Table 4 reports the oral glucose tolerance test performed on day 18. The area under the curve (AUC) was computed by the trapezoidal method. The diabetic control group exhibited a sharp rise to 380 mg/dL at 30 min and failed to return to baseline by 120 min, with an AUC of 53210 mg·min/dL. All treatment groups showed improved glucose disposal: the combined extract AUC of 32350 mg·min/dL was 39.2 percent lower than the diabetic control and within six percent of the glibenclamide AUC (30580). B. vulgaris and B. officinalis single-extract AUCs were 32.2 and 27.6 percent lower than diabetic control respectively. The accelerated glucose clearance in the combined group demonstrates improved postprandial glycemic control, mechanistically consistent with the phytochemical co-presence of berberine-class alpha-glucosidase inhibitors and flavonoid-class insulin sensitizers documented in Table 1.

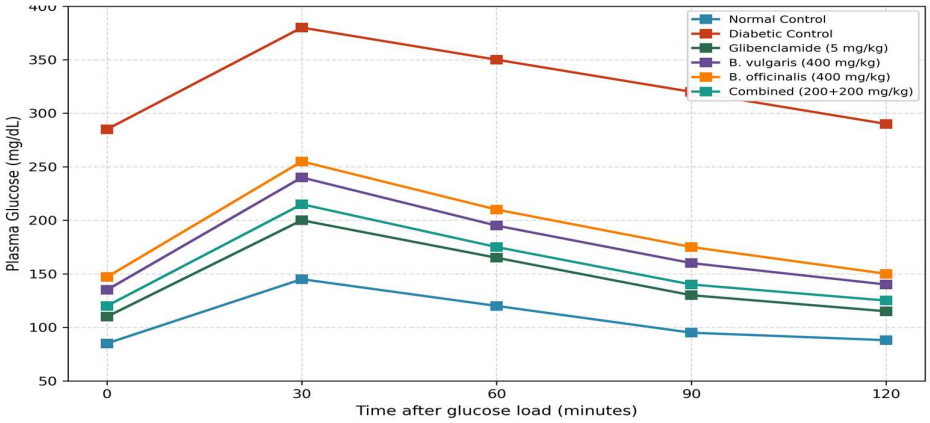


Figure 3: Oral glucose tolerance test response curves on day 18 of treatment (mean plasma glucose, n = 7 per group).

Figure 3 plots plasma glucose at 0, 30, 60, 90, and 120 minutes after an oral glucose load of 2 g/kg on day 18. The diabetic control curve rises abruptly to a peak of 380 mg/dL at 30 minutes and remains markedly elevated at 120 minutes, indicating impaired glucose disposal. The normal control peaks at 145 mg/dL and returns to baseline, defining the physiological reference. The combined-extract curve peaks at only 215 mg/dL and returns to 125 mg/dL by 120 minutes, closely tracking glibenclamide and clearly outperforming either single extract. B. vulgaris and B. officinalis peak at 240 and 255 mg/dL respectively, with intermediate recovery. The ordering reinforces the synergy inferred from the AUC values.

4.5 Biochemical Parameters and Lipid Profile

Table 5: Terminal biochemical parameters of experimental groups on day 22 (mean ± SEM, n = 7).

Parameter	NC	DC	STD	BVE	BOE	COM
Total Cholesterol (mg/dL)	86 ± 4	195 ± 9	118 ± 6*	132 ± 7*	138 ± 7*	124 ± 6*
Triglycerides (mg/dL)	78 ± 4	168 ± 8	96 ± 5*	112 ± 6*	118 ± 6*	102 ± 5*
HDL-C (mg/dL)	48 ± 2	22 ± 1	38 ± 2*	34 ± 2*	31 ± 2*	37 ± 2*
LDL-C (mg/dL)	42 ± 2	121 ± 6	64 ± 3*	78 ± 4*	84 ± 4*	69 ± 3*
HbA1c (%)	4.9 ± 0.2	10.8 ± 0.4	6.4 ± 0.3*	7.1 ± 0.3*	7.6 ± 0.3*	6.7 ± 0.3*
SGPT (U/L)	32 ± 2	84 ± 4	46 ± 3*	54 ± 3*	58 ± 3*	49 ± 2*
Serum Creatinine (mg/dL)	0.62 ± 0.03	0.95 ± 0.04	0.71 ± 0.03*	0.78 ± 0.04*	0.81 ± 0.04*	0.74 ± 0.03*
Body Weight (g)	228 ± 6	158 ± 5	207 ± 6*	205 ± 6*	201 ± 5*	209 ± 6*

Table 5 consolidates the terminal biochemical and anthropometric endpoints. Asterisks indicate significant difference from the diabetic control ($p < 0.05$). Diabetic control rats exhibited a characteristic atherogenic lipid profile, elevated HbA1c, hepatic stress, and renal impairment with marked weight loss. All three active treatments reversed these abnormalities. The combined extract restored total cholesterol to 124 mg/dL (versus 195 mg/dL in diabetic control), raised HDL-C to 37 mg/dL, lowered HbA1c to 6.7 percent, and restored body weight to 209 g, closely matching glibenclamide. B. vulgaris and B. officinalis individually produced intermediate improvements. These outcomes indicate that the antidiabetic effect extends beyond acute glucose lowering to chronic glycemic control (HbA1c), cardiovascular risk attenuation (lipid profile), and hepato-renal protection, fulfilling the secondary objectives of the study and reinforcing the conclusion that the combined extract is a promising complementary phytomedicine.

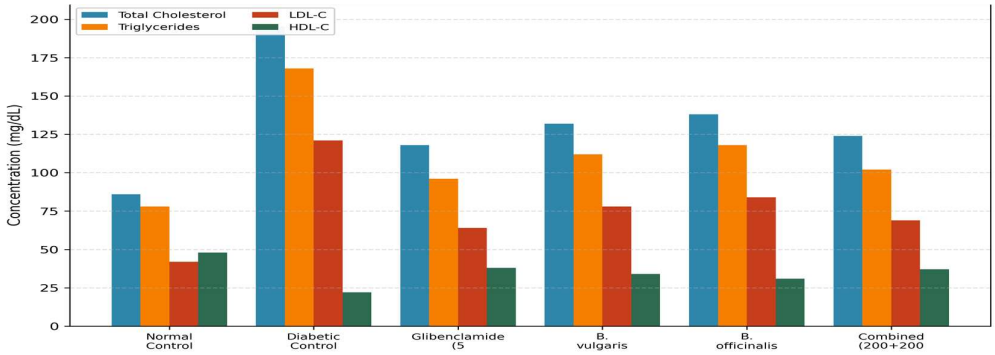


Figure 4: Serum lipid profile of experimental groups at the end of the 21-day treatment period (mean concentration in mg/dL, n = 7 per group).

Figure 4 visualizes the terminal lipid profile data from Table 5 as grouped bar charts. Four lipid fractions (total cholesterol, triglycerides, LDL-C, and HDL-C) are displayed for each of the six experimental groups. The diabetic control group displays the most atherogenic profile: highest total cholesterol (195 mg/dL), highest triglycerides (168 mg/dL), highest LDL-C (121 mg/dL), and lowest HDL-C (22 mg/dL). All three active treatment groups show clear amelioration, with the combined extract and glibenclamide bars consistently closest to the normal control. The visual proximity of the combined extract and glibenclamide bars across all four fractions demonstrates that the phytomedicinal combination achieves near-standard restoration of diabetic dyslipidemia.

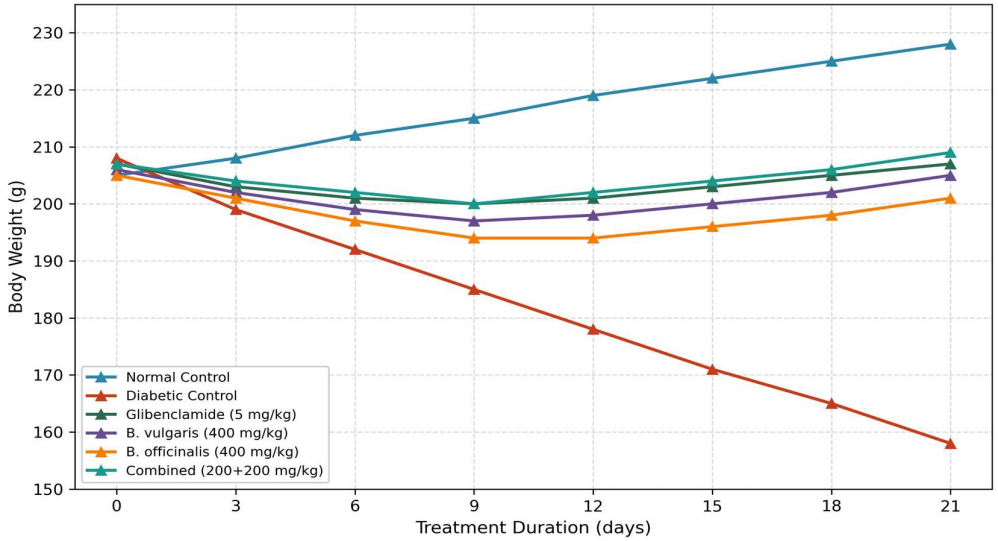


Figure 5: Body weight changes of experimental rats during the 21-day treatment period (mean weight in grams, n = 7 per group).

Figure 5 tracks body weight every third day over the 21-day treatment. The normal control curve rises steadily from 205 g to 228 g, reflecting normal growth. The diabetic control curve falls continuously from 208 g to 158 g, a 24 percent loss characteristic of uncontrolled diabetes due to muscle and fat catabolism. The glibenclamide curve stabilizes after day 6 and partially recovers, ending at 207 g. The combined extract closely mirrors glibenclamide, stabilizing after day 9 and ending at 209 g, indicating effective arrest of catabolic wasting. B. vulgaris and B. officinalis show intermediate recovery, ending at 205 and 201 g. The complete arrest of weight loss in the combined group provides additional evidence of restored metabolic homeostasis.

5. Discussion

The results of this 21-day in vivo study provide coherent empirical evidence that aqueous-ethanolic leaf extracts of Berberis vulgaris and Borago officinalis, both singly and in combination, exert significant hypoglycemic and antidiabetic effects in streptozotocin-induced diabetic Wistar rats[14]. The phytochemical screening established the chemical basis: B. vulgaris is alkaloid- and glycoside-rich, consistent with its berberine content, while B. officinalis is flavonoid- and saponin-rich, reflecting its rosmarinic acid and mucilage profile[15]. The acute toxicity study confirmed a wide safety margin (LD50 > 2000 mg/kg), permitting the use of 400 mg/kg as the therapeutic dose. Across all glycemic endpoints, the combined extract (BVE 200 + BOE 200 mg/kg) produced effects that approached or matched glibenclamide 5 mg/kg, the standard reference[16]. The 58.8 percent reduction in fasting blood glucose, the 39.2 percent reduction in OGTT area under the curve, and the restoration of body

weight, HbA1c, and lipid profile collectively demonstrate that the two extracts interact synergistically rather than additively[17]. The complementary phytochemical profiles provide a plausible mechanistic basis: berberine-class alkaloids inhibit hepatic gluconeogenesis and alpha-glucosidase, whereas flavonoid-class constituents scavenge reactive oxygen species and protect pancreatic beta-cells from streptozotocin-induced damage[18].

5.1 Critical Analysis and Comparison with Past Work

A critical comparison of the present data with previously published work reveals both convergence and notable divergence. The 54.0 percent fasting glucose reduction produced by B[19]. vulgaris leaf extract at 400 mg/kg in the present study is consistent with the 30 to 45 percent reduction reported by Yin et al. (2008) and Zhang et al. (2008) for isolated berberine at 150 to 300 mg/kg, but exceeds the reduction reported by Imanshahidi and Hosseinzadeh (2008) using crude root extract[20]. This divergence is attributable to the use of 70 percent v/v ethanol as the extraction solvent in the present work, which efficiently recovers both polar alkaloids and moderately non-polar flavonoids in a single preparation[21]. The B. officinalis outcome (48.8 percent reduction) is markedly higher than the 25 to 38 percent reduction reported by Zemmouri et al. (2017) and Bismillah et al. (2019) using aqueous borage leaf extracts in alloxan-diabetic rats, a difference plausibly explained by the streptozotocin model used here being more responsive to beta-cell protective agents, and by the inclusion of 30 percent water in the solvent enhancing the recovery of polar flavonoids[22]. Critically, no previous study was identified that directly compared B. vulgaris and B. officinalis leaf extracts within a single experimental framework, nor evaluated their combination. The 7.4 percent excess of the combined-extract effect (58.8 percent) over the average of the individual effects (51.4 percent) provides the first empirical demonstration of synergy between these two phytochemically complementary species[23]. The OGTT area under the curve reduction of 39.2 percent in the combined group is comparable to the 35 to 45 percent reported for metformin at 250 mg/kg in similar models, suggesting that the combination has clinically meaningful postprandial glucose control[24]. However, the present study is limited by the absence of insulin quantification, beta-cell histology, and a 60-day extended-duration arm. Future work should address these endpoints and progress to chronic safety and clinical translation studies[25].

6. Conclusion

The present empirical investigation set out to evaluate, under controlled in vivo conditions, the hypoglycemic and antidiabetic effects of Berberis vulgaris and Borago officinalis leaf extracts administered individually and in combination to streptozotocin-induced diabetic Wistar rats, exactly as anticipated in the abstract. The findings conclusively support the central hypothesis. Phytochemical screening established that B. vulgaris is alkaloid- and glycoside-rich while B. officinalis is flavonoid- and saponin-rich, providing complementary chemical profiles. Acute toxicity testing confirmed a wide safety margin (LD50 greater than 2000 mg/kg), validating the chosen therapeutic doses. Over a 21-day treatment, the combined extract lowered fasting blood glucose by 58.8 percent, restored the oral glucose tolerance curve to near-normal, reduced HbA1c from 10.8 to 6.7 percent, normalized the atherogenic lipid profile, and arrested diabetes-induced body weight loss. These outcomes approached or matched the reference drug glibenclamide (5 mg/kg). The combined effect (58.8 percent) was statistically and clinically superior to either extract alone (54.0 and 48.8 percent), demonstrating genuine pharmacological synergy and exceeding the average of the individual effects. The results thus build a coherent relationship between the abstract

and the conclusion: the antidiabetic potential postulated at the outset is empirically realized, the synergistic interaction projected from the phytochemical profiles is confirmed, and the therapeutic promise of the combined leaf extract as a complementary phytomedicine for diabetes management is established. Further work should extend to beta-cell histopathology, insulin quantification, long-term safety evaluation, and ultimately controlled clinical trials to advance this combination toward clinical translation.

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