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ORIGINAL RESEARCH

# Evaluation of in vivo Antidiabetic, Antidyslipidemic and in vitro Anti-Oxidant Activity of Extract and Solvent Fractions of *Discopodium penninervum Hoschst* Leaf in Mice: Normoglycemic and Streptozocin-Induced Model

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**Background:** Diabetes mellitus has become a huge global public health and economic issue. The shortcomings of current medicines, as well as their serious side effects, prompted a focused quest for natural medicinal agents. In Ethiopia, the leaf of *Discopodium penninervum Hoschst* has been utilized in the traditional health system to treat diabetes. The goal of this study was to confirm the anti-diabetic, anti-dyslipidemia, and anti-oxidant activity of *Discopodium penninervum Hoschst* leaf in both in vitro and in vivo.

**Methods:** In the normoglycemic, glucose-loaded, and streptozotocin-induced diabetic mouse models, the blood glucose-lowering effects of extract and solvent fractions of the leaf of *Discopodium penninervum Hoschst* were tested. The weight and lipid profile of streptozotocin-induced diabetic mice were assessed after treatment with leaf extract and solvent fractions for 14 days. The DPPH test was used to assess the antioxidant activity of the plant leaf extract.

**Results:** In the normoglycemic model and glucose loaded test, the leaf extract of *Discopodium penninervum Hoschst* demonstrated significant blood glucose decrease (34.1%, $p<0.001$) and 44.5%, $p<0.001$, respectively, when compared to the normal control. When compared to a diabetic control group, extract and solvent fractions significantly ($p<0.001$) reduced blood glucose levels on the 14th day in the streptozotocin-induced diabetic model. In addition, serum TC, STG, TG, LDL, and VLDL levels were reduced significantly ($p<0.001$). IC50 values of leaf extract and a standard medication (ascorbic acid) in the antioxidant activity test were 4.1g/mL and 10.23g/mL, respectively.

**Conclusion:** The hydro-alcoholic leaf extract and solvent fractions of *Discopodium penninervum Hoschst* leaves have demonstrated blood glucose-lowering effect, which justify ethnobotanical use, and can therefore be used as a good insight for new anti-diabetic medication source with a call for additional studies.

**Keywords:** diabetic mellitus, *Discopodium penninervum Hoschst*, streptozotocin, blood glucose level

## Introduction

### Background

Diabetes mellitus (DM) is a serious, chronic, and heterogeneous group of metabolic disorders characterized by persistent hyperglycemia due to changes in carbohydrate, fat, and protein metabolism caused by inherited and/or acquired insulin deficiency and ineffectiveness of insulin produced by Beta cells and long term hyperglycemia during diabetes is linked to eye, kidney, nerve, and heart dysfunction, as well as diabetic foot ulcers.[1,2] It has been reported from an IDF; in 2019 around 463 million people were with diabetes in the world, also it will rise to 578 and 700 million people by 2030 and 2045, respectively. The basic characteristics of DM include hyperglycemia, hyperlipidemia, and oxidative stress, which



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are all substantial risk factors for the development of diabetes complications.[3] As a result, therapeutic alternatives containing antihyperglycemic, antihyperlipidemic, and antioxidant activities with proven long-term safety should be targeted from natural products in a clinical setting for patients with coexisting diabetes and metabolic disorders, and it is also the WHO's recommendation to derive new antidiabetic drugs from natural products that are both safe and effective for the treatment of diabetes mellitus.[4] The inadequacies of conventional medicines, as well as serious side effects with insulin therapy and oral antidiabetic agents, prompted a determined search for natural therapeutic agents. Because these first-line treatments for diabetes mellitus have some side effects and fail to significantly alter the course of diabetic complications, a determined search for alternative natural therapeutic agents ensued.[5] Furthermore, the lack of efficacy and safety of currently available oral anti-diabetic medications, combined with the disease's emergence as a global epidemic, has prompted the development of new therapies that can better treat diabetes.[6] The use of STZ to cause diabetes in rat models is widely established, and STZ-induced diabetes is said to resemble human DM, which is distinguished from normal rodents by body weight loss, glycosuria, hyperglycemia, polyphagia, and polydipsia.[7] Due to STZ's toxic effect on pancreatic -cells, which causes a reduction in insulin secretion, and because it is a structural analog of glucose, it is taken up by pancreatic -cells through GLUT 2 and kills beta cells through DNA methylation and free radical generation in experimental diabetes in animals.[8] After being harmed by toxins (STZ, alloxan), the pancreas includes stable (quiescent) -cells that can regenerate through neogenesis or replication of the already differentiated cells. Free radicals are detrimental to human health because they destroy and mutate cells.[9] Consumption of naturally occurring substances, including as grains, pulses, nuts, fruits, and vegetables that have antioxidant activity, has increased recently. Antioxidants play a vital role in preventing them.[10] Natural goods have garnered a lot of attention as sources of bioactive compounds, including antioxidants, and their antioxidant action has positive effects on maintaining beta cell function in diabetes. Natural products also play a significant role in the identification of new therapeutic agents.[11] The development of many diseases, including diabetes mellitus and its consequences, involves the induction of oxidative stress. Various studies have described how antioxidants can treat diabetes and its complications by preventing oxidative stress.[12] *Discopodium penninervum Hoschst*, one of the medicinal plants used in the local treatment of diabetes by eat the boiled leaf as a cabbage in Ethiopia and also it is one of those plants used to manage diabetes without scientific validation, and the plant belongs to the Solanaceae family.[13–16] Local names for the solanaceous plant *Discopodium penninervum Hochst* in Ethiopia include alumi (Agawgna), ameraro (Amaharic), and mararo (Oromiffa). It is a tiny tree or shrub with a maximum height of 5 meters, slightly mushy stems, and brown and hairy branchlets.[17] Three 16-oxygenated with anolides that were isolated from the leaves of this plant were studied for their cytotoxicity and immunosuppressive properties. The results revealed that jaborosalactone-L has cytotoxicity only for the murine macrophage cell line, RAW 264.7, whereas the 16-oxygenated withanolides showed cytotoxicity to both human (COR-L23 and ECV 304) and murine (L929 and RAW 264.7) cells.[18] According to current results, compounds having cytotoxic properties are medically advised for antidiabetic activity. This plant has been shown to have a cytotoxic impact in vitro.[19] In Ethiopian traditional medicine, the *Discopodium penninervum Hoschst* leaf has been used to cure cancer, schistosomiasis, stomachache, leprosy, dermatitis, and liver illness, in addition to Diabetes mellitus.[20,21] There are no previous scientific findings on the in vivo antidiabetic, antihyperlipidemic, and in vitro antioxidant activity of *Discopodium penninervum Hoschst* leaf in mice that the authors are aware of. Thus, the goal of this study was to determine the in vivo antidiabetic, antihyperlipidemic, and in vitro antioxidant properties of *Discopodium penninervum Hoschst* leaf extract and solvent fractions in mice.

# Methods and Materials

## Chemicals and Instruments

DPPH (Sigma-Aldrich, Germany), sodium citrate (Lab tech chemicals, India), methanol (Nice chemicals, India), 5% glucose solution (Reyoung pharmaceuticals, China), Whatman filter paper No.1, test tube, beakers, funnels, measuring cylinder, glass rod, spatula, pipettes, gavages (oral feeding syringes), Syringes (1 mL, 3 mL, and 5 mL) with needles, desiccators, digital analytical balance (EPH-400 Abron Exports), pH meter (Bante Instruments, UK), Hot air oven (Medit-Medizin Technik, Germany), Automated chemistry analyzer (Beckman Coulter, Germany), UV-spectrophotometer (Agilent Technologies,

Malaysia), rotary evaporator (Hamato, Japan), Tween-80 (Avishkar Lab Tech chemicals, India), Streptozotocin (Fisco Research laboratories, India), glibenclamide (Julphar pharmaceuticals, Ethiopia), ascorbic acid (Blulux Labratories, Inida), Sensor Card glucometer and strip (Alliance international, Taiwan), Lyophilizer (Labfreez, China), ethyl acetate (Loba chemie, India), chloroform (Aristar, England), sodium hydroxide (Blulux Laboratories, India).

## Plant Material

*Discopodium penninervum Hoschst* fresh leaves were obtained from D/Togo kebele in the Dega district (located in Buno Bedelle Zone of Oromia Region, southwest Ethiopia). Botanists identified and authenticated the plant material, and the voucher specimen (004/WWJ/2022) was deposited in the Biology department of Mettu University's College of Natural and Computational Science.

## Extraction and Fractionation

### Preparation of Plant Extract

In an erlenmeyer flask, 1.8 kg of powder was macerated for 72 hours in 80% methanol which means 20% of it was aqueous solvent (250 g in 1500 mL) with intermittent stirring at room temperature. The mixture was filtered twice, first with a muslin cloth and then with Whatman filters paper No. 1 after 72 hours. The filtrate was maintained at 4°C in the refrigerator, while the marc was macerated twice for 72 hours each time with the same volume of 80% methanol to extract the plant material completely. A rotary evaporator was used to concentrate the combined filtrate obtained from consecutive maceration under decreasing pressure (Hamato, Japan). The extract was then freeze-dried to eliminate the water solvent using a lyophilizer (Labfreez, China).[22]

### Preparation of Plant Fractions

The leaf extract was fractionated using water, ethyl acetate, and chloroform as solvents. The plant extract was suspended in 400 mL distilled water before being transferred to a separating funnel. It was then filled with an equal amount of chloroform and forcefully shaken. The mixture was separated into two layers: chloroform and aqueous, with the chloroform layer being removed first. The chloroform partition was carried out twice more in the same way. To obtain the chloroform fraction, the chloroform layer was mixed and evaporated in a hot air oven set at 40°C. Next to that, 400mL ethyl acetate was added to the separating funnel containing the aqueous layer and the same procedure was followed as with chloroform fraction. After the ethyl acetate layer was removed and the aqueous layer was added, the mixture formed two layers then, the residual aqueous layer was concentrated in a hot air oven set at 40°C, then frozen overnight in the refrigerator before being concentrated in a lyophilizer to remove the water. The dried fractions' percent yield was estimated, and the fractions were placed in airtight bottles and stored in the refrigerator at 4°C until needed.[23]

## Experimental Animals

Male mice were used in all of the models used in this investigation, with the exception of acute oral toxicity, because male mice are more sensitive to STZ and insulin than female mice.[24] In the study, healthy male Swiss albino mice (weighing 20–30 g and aged 6–10 weeks) were employed.[25] The pharmacy department of Mettu University provided the animals. The animals were housed in polypropylene cages (6–10 animals per cage) with a pellet feed and unlimited access to water in regular settings (12 hours of light and 12 hours of darkness). One week before the experiment started, they were accustomed to the lab's environment. The Department of Pharmacy at Mettu University's research and ethics committee approved all experiments in accordance with the National Academy of Sciences' National Academy of Sciences Guide for the Care and Use of Laboratory Animals, 8th edition (2011), published by the National Academy of Sciences, Institute for Laboratory Animal Research, Division on Earth and Life Studies in Washington, DC, USA.[26]

## Phytochemical Screening Effect of Leaf Extract and Solvent Fractions

Secondary metabolites such as alkaloids, steroidal compounds, phenolic compounds, tannin, saponins, terpenes, and flavonoids were screened for the presence or absence in leaf extract and solvent fractions of *Discopodium penninervum Hoschst* using standard procedures.[27]

## Acute Oral Toxicity Test

The OECD 425 guideline limit test protocol was used to conduct an acute oral toxicity test.[28] On the first day, one mouse was fasted for 3 hours before receiving the leaf extract/solvent fractions at a dose of 2000 mg/kg. The mouse was then watched for physical, neurological, autonomic, or behavioral abnormalities at least once within the first 30 minutes, on a regular basis for the next 24 hours, with a focus on the first 4 hours, and for the next 24 hours. Following the first mouse's results, the next four mice were enlisted, fasted for 3–4 hours, and given a single dosage of 2000 mg/kg before being watched in the same way. They were monitored for a total of 14 days to see if they showed any signs of illness.

## Grouping and Dosing of Animals

Swiss albino male mice were fasted for 4–6 hours in the morning for both the normoglycemic and glucose-loaded mouse models, although water was available ad libitum, and then randomly divided into five groups (6 mice per group). Group I was given 10mL/kg of distilled water, group II was given 5mg/kg of glibenclamide, and the remaining three groups (III, IV, and V) were given 100, 200, and 400 mg/kg of extract, respectively.

Mice were starved overnight for 14 hours and divided into 15 groups randomly in the single-dose STZ-induced experiment (each group contained six mice). Then, group I was given a vehicle (distilled water for the aqueous fraction and leaf extract), group II was given a vehicle (2% tween-80 for the ethyl acetate and chloroform fractions), group III was given glibenclamide 5 mg/kg, and the remaining groups were given different doses of *Discopodium penninervum Hoschst* leaf extract (100, 200, and 400 mg/kg); aqueous fraction (100, 200, and 400mg/kg); ethyl acetate (100, 200 and 400mg/kg) and chloroform fraction (100, 200, and 400mg/kg).

The STZ-induced mice were treated with a daily dose leaf extract and solvent fractions for two weeks. Mice were divided into 14 groups at random after fasting for 14 hours. Group I received vehicle (distilled water for both aqueous fraction and leaf extract, diabetic control), group II received vehicle (2% tween-80 for ethyl acetate fractions, diabetic control), group III received vehicle (2% tween-80 for ethyl acetate, normal control), group IV received vehicle (distilled water for aqueous fraction and leaf extract, normal control), group V, received glibenclamide 5mg/kg and the remaining groups received different dose of the *Discopodium penninervum Hoschst* leaf extract (100, 200, and 400mg/kg); aqueous fraction (100, 200, and 400mg/kg), and ethyl acetate fraction (100, 200 and 400 mg/kg).[29]

## Induction of Experimental Diabetes

Before the development of diabetes, the male Swiss albino mice were fasted for 16 hours and their body weights were recorded. A single intraperitoneal dose of 150 mg/kg of STZ was used to produce experimental diabetes.[30] Mice were screened for the development of diabetes 3 days after receiving STZ injection, and those with a fasting blood glucose level of more than 200 mg/dl were included in the study as diabetes mice and randomly assigned to different groups.[31]

## Effect of Leaf Extract of *Discopodium penninervum Hoschst* on Blood Glucose Level of Normal Fasted Mice

Mice were divided into groups and given treatments as indicated in Grouping and Dosing of Animals. To assess BGL, a blood sample was taken from the tips of each mouse's tail vein under aseptic circumstances. Just before treatment, each mouse's blood glucose level was tested (0 hours) After that, each mouse's blood glucose level was monitored at 1, 2, 3, and 4 hours after treatment.[32]

## Effect of Leaf Extract of *Discopodium penninervum Hoschst* on Post Prandial Glycemia in Normal Fasted Mice

Mice were divided into groups and given treatments as indicated in Grouping and Dosing of Animals. All of the mice were given a 2 g/kg glucose solution orally 30 minutes before extract therapy, and blood samples were taken before treatment (ie, 0 minutes), 30, 60, and 120 minutes following extract administration to assess their blood glucose levels.[33]

### The Antihyperglycemic Activity of a Single Dose of the Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* on Streptozocin-Induced Mice

Mice were divided into groups and given treatments as indicated in Grouping and Dosing of Animals. BGL was assessed at two time points: before treatment (0 hours) and 2, 4, 6, and 8 hours after treatment.[34]

### Antihyperglycemic Activity of Repeated Daily Dose of Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* on Streptozocin-Induced Mice

Following a 14-hour overnight fast, mice's fasting blood glucose level and body weight were measured on day 0 (before treatment), day 7, and day 14 of therapy. On the 15th day, blood was obtained in a sterile tube from over fasted (14 hours) diabetes mice through heart puncture under halothane anesthesia. After 2 hours at room temperature, the blood sample was centrifuged and the supernatant was removed from the pellet as soon as possible to prepare serum samples for analysis of TG, TC, HDL, VLD, and LDL using an automated chemical analyzer.[33,35]

### Antioxidant Activity of Leaf Extract of *Discopodium penninervum Hoschst* in Diphenyl-2-Picrylhydrazyl Assay

The plant leaf extract's free radical scavenging activity was measured using the method published by Brand William et al.[36] The scavenging activity of the stable DPPH free radical was used to estimate the possible antioxidant activity of leaf extract. The DPPH solution was produced (as 4mg of DPPH and dissolved in absolute methanol of 100mL, each time freshly prepared and stored in a dark and cool place). Six milligrams of ascorbic acid was dissolved in 3 mL 100% methanol to make an ascorbic acid solution (6000 g/3 mL, stock solution). Then, 15.625, 31.25, 62.5, 125, 250, and 500 g/mL dilutions were made from the stock solution. To summarize, 100 µL of test sample solution dissolved in methanol at various concentrations (500, 250, 125, 62.5, 31.25, and 15.625 g/mL) were generated from the plant's leaf extract and then transferred to a separate test tube containing 3.9 mL of a 0.004% (w/v) DPPH radicals dissolved in methanol in separate test tubes. After 30 minutes, the absorbance at 517 nm was measured, and the percent inhibitory activity was computed. The IC50 value is the sample concentration necessary to scavenge 50% of DPPH-free radicals.

### Statistical Analysis

The results were presented as mean ± standard error of means (SEM) for six mice in each group. One-way ANOVA was used to compare the means of all parameters across groups and between and within groups, followed by Tukey's multiple comparison tests.

## Results

### The Percentage Yield of Plant Material

Products of leaf extract and solvent fractionations were 80.2g (10.8%), 28g (39.2%,), 10g (16.5%), and 26.4g (36.3%,) of leaf extract, ethyl acetate, chloroform, and aqueous fractions, respectively.

### Acute Toxicity Test

The mice did not display any indicators of toxicity such as lacrimation, hair erection, convulsion, coma, or death after a single oral dosage of 2000 mg/kg of *Discopodium penninervum Hoschst* during the 24-hour follow-up as well as the 14-day observation period. This verifies that *Discopodium penninervum Hoschst's* LD50 is greater than 2g/kg.

### Phytochemical Screening Effect of Leaf Extract and Solvent Fractions

Tannins, flavonoids, terpenoids, phenolic compounds, saponins, and anthraquinones were found in the phytochemical screening of *Discopodium penninervum Hoschst*, as indicated in Table 1.

**Table 1** Phytochemical Screening Effect of the Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst*

| Leaf Extract and Fraction | | | | |
|---|---|---|---|---|
| **Phyto-Compounds** | **Leaf Extract** | **Aqueous Fraction** | **Ethyl Acetate Fraction** | **Chloroform Fraction** |
| Alkaloids | _ | _ | + | _ |
| Flavonoids | + | + | + | + |
| Phenols | + | + | + | + |
| Tannins | + | + | + | + |
| Saponins | + | + | + | _ |
| Steroid | _ | _ | + | + |
| Anthraquinones | + | + | + | _ |
| Cardiac glycosides | + | + | + | _ |
| Terpenoids | + | _ | _ | _ |

**Note**: (+): detected, (-): not detected.

## Effect of Leaf Extract of *Discopodium penninervum Hoschst* on Normal Fasted Mice

Table 2 shows the effect of *Discopodium penninervum Hoschst* leaf extract on blood glucose levels in normal fasting mice. Except for the first hour after exposure, the overall reduction in BGL was substantial ($p < 0.001$). When compared to the initial or baseline level, DW 10mL-treated mice demonstrated a substantial drop in BGL at the 4th hr time points. Intragroup comparisons demonstrated significant ($p<0.001$) BGL reductions in the 200 mg/kg- and 400 mg/kg-treated groups during the 3rd and 4th hours of treatment compared to the baseline BGL. In this study, the maximum BGL reduction was 34.1% ($p<0.001$) and 29% ($p<0.001$) at the 4th hour for 200 mg/kg and 200 mg/kg, respectively.

## Effect of Leaf Extract of *Discopodium penninervum Hoschst* on Post Prandial Glycemia in Normal Mice

Table 3 summarizes the effects of *Discopodium penninervum Hoschst* leaf extract on post prandial glycemia in non diabetic mice. The delivery of glucose (2g/kg) to the mice resulted in a peak BGL 1 hour after glucose loading, confirming hyperglycemia induction. When compared to the control group, the extract at three doses (100, 200, and 400 mg/kg) exhibited a substantial reduction in BGL from 60 minutes onwards. Furthermore, when the different doses of the extract were compared to each other as well as the positive control at all-time points; however, no discernible difference was found.

**Table 2** Effect of Leaf Extract of *Discopodium penninervum Hoschst* on Blood Glucose Level of Normal Mice

| Groups | Blood Glucose Level in mg/dl | | | | |
|---|---|---|---|---|---|
| | **0 Hour** | **1 Hour** | **2 Hours** | **3 Hours** | **4 Hours** |
| DW 10mL | 90.66±2.2 | 89.50±4 | 88.5±3.5 | 87.83±1.8 | 85.3±4.8 |
| DP100mg | 93.00±4.7 | 87.3±5.2***$^{a}$***$^{b}$***$^{c}$ | 78.50±2.1***$^{a}$***$^{b}$***$^{c}$ | 71.7±4.7***$^{a}$***$^{b}$***$^{c}$***$^{f}$ | 71.8±2.5***$^{a}$***$^{b}$***$^{c}$***$^{f}$ |
| DP200mg | 98.4±5.4 | 80.6±4.3***$^{a}$***$^{b}$***$^{c}$***$^{f}$ | 78.33±1.7***$^{a}$***$^{b}$***$^{c}$***$^{f}$ | 67.5±3.2***$^{a}$***$^{b}$***$^{c}$***$^{d}$ | 64.3±3.3***$^{a}$***$^{b}$***$^{c}$***$^{d}$ |
| DP400mg | 94.50±3.6 | 83.66±4.55***$^{a}$***$^{b}$***$^{c}$***$^{e}$ | 72.50±2.2***$^{a}$***$^{b}$***$^{c}$***$^{e}$ | 67.50±5.8***$^{a}$***$^{b}$***$^{c}$ | 65.50±2.7***$^{a}$***$^{b}$***$^{c}$***$^{d}$ |
| GLC 5mg | 93.30±2.9 | 62.5±3.5***$^{a}$***$^{c}$***$^{d}$***$^{e}$**$^{f}$ | 58.44±2.4***$^{a}$***$^{c}$***$^{d}$***$^{e}$**$^{f}$ | 55.12±5.5***$^{a}$***$^{c}$***$^{d}$***$^{e}$**$^{f}$ | 54.50±1.3***$^{a}$***$^{c}$***$^{d}$***$^{e}$**$^{f}$ |

**Notes**: Each values represents mean ± SEM (n=6). a = compared to the normal control; c = compared to baseline blood glucose level; d = compared to 100mg; e = compared to 200mg; f = compared to 400mg. * = $p<0.05$; ** = $p<0.01$; and *** = $p<0.001$.
**Abbreviations**: DP, *Discopodium penninervum*; GLC, glibenclamide; DW, distilled water.

**Table 3** Effects of the Leaf Extract of *Discopodium penninervum Hoschst* on Post Prandial Glycaemia in Normal Mice

| Groups | Blood Glucose Level in mg/dl | | | |
|---|---|---|---|---|
| | 0 Minutes | 30 Minutes | 60 Minutes | 120 Minutes |
| DW10ml | 85.1±6.6 | 128.7±5.4 | 122.5±4.3$^{*c}$ | 116.20±2.9$^{**c}$ |
| DP100mg<br>DP200mg<br>DP400mg | 82.22±4.4<br>87.3±4.9<br>88.5±6.0 | 133.3±3.1<br>139.5±6.5<br>143.3±7.6 | 87.1±5.7$^{***a***b***c***f}$<br>73.5±5.4$^{***a***b***c***d***f}$<br>90.1±5.1$^{***a***b***c***d***e}$ | 70.6±8.0$^{***a***b***c***f}$<br>63.0±7.5$^{***a***b***c***d***f}$<br>79.50±7.6$^{***a***b***c***d***e}$ |
| GLC5mg | 84.31±5.5 | 128.61±4.7 | 77.1±3.2$^{***a***c***d***e***f}$ | 60.61±1.5$^{***a***c***d***e***f}$ |

**Note**: Each values represents mean ± SEM (n=6). a = compared to the normal control; c = compared to 30 minutes; d = compared to 100mg; e = compared to 200mg. *p<0.05; **p<0.01, and ***p<0.001.
**Abbreviations**: DP, *Discopodium penninervum*; GLC, glibenclamide; DW, distilled water; NC, normal control.

## Antihyperglycemic Activity of a Single Dose of the Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* in Diabetic Mice

In diabetic mice, the antihyperglycemic activity of a single dose of the leaf extract and solvent fractions was investigated, and the results are reported in Table 4. Across all groups, there was no significant difference in baseline blood glucose levels. When groups receiving the plant extract and solvent fraction were compared to each other, there was no significant difference in blood glucose levels at any time point. Table 4 shows that when compared to diabetes control, the leaf extract, aqueous fraction, and ethyl acetate showed significant (p<0.001) BGL reduction at all doses after 4 hours of therapy. Furthermore, when compared to baseline and diabetes control data, the chloroform fraction showed a significant (p< 0.001) drop in BGL after 8 hours of therapy at a dose of 400mg/kg. Likewise, as compared to the diabetic control, the standard treatment (GLC 5 mg/kg) resulted in significant BGL reductions at 2 hours (P<0.001), 4 hours (P<001), 6 hours (P<0.001), and 8 hours

**Table 4** Single Dose Antihyperglycemic Effect of Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* on Streptozocin Diabetic Mice

| Group | Blood Glucose Level in mg/dl | | | | |
|---|---|---|---|---|---|
| | 0 Hour | 2 Hours | 4 Hours | 6 Hours | 8 Hours |
| DCDW10ml | 335.5±1.8 | 348.0±9.3 | 350.6±7.1 | 353.3±8.4 | 357.5±4.2 |
| DP100mg<br>DP200mg<br>DP 400mg | 330.3±2.1<br>320.8±1.16<br>323.7±2.3 | 300.3±2.5<br>281.6±6.7$^{***b}$<br>286.50±4.6$^{***b}$ | 234.6±8.8<br>245.6±8.8$^{***a***b}$<br>250.7±2.6$^{***a***b}$ | 223±5.7$^{**a**b}$<br>210.6±6.2$^{***a***b}$<br>190.6±6.2$^{***a***b}$ | 200.1±7.10$^{**a**b}$<br>190.50±7.6$^{***a***b}$<br>172.50±5.3$^{***a***b}$ |
| AF100mg<br>AF200mg<br>AF400mg | 328.31±8.8<br>334.4±7.5<br>331.00±6.4 | 293.00±1.06<br>283.5±3.4$^{***b}$<br>295.50±6.4$^{***b}$ | 220.3±3.3<br>230.75±3.9$^{***b***a}$<br>246.00±5.00$^{***a***b}$ | 210.8±9.4$^{**a**b}$<br>200.20±3.2$^{***a***b}$<br>182.16±4.65$^{***a***b}$ | 188.3±8.8$^{**a**b}$<br>180.40±4.1$^{***a***b}$<br>176.83±7.2$^{***a***b}$ |
| EF100mg<br>EF200mg<br>EF400mg | 325.77±4.5<br>320.83±4.7<br>322.5±2.5 | 280.0±9.6<br>281.00±5.7$^{***b}$<br>295.50±3.5$^{***b}$ | 218.50±6.2<br>227.50±9.5$^{***a***b}$<br>243.5±7.6$^{***a***b}$ | 205.00±6.1<br>187.66±8.9$^{***a***b}$<br>206.0±1.6$^{***a***b}$ | 182.66±6.6<br>170.66±8.8$^{***a***b}$<br>169.50±7.6$^{***a***b}$ |
| CF100mg<br>CF200mg<br>CF400mg | 320.3±2.4<br>318.50±4.7<br>316.6±5.1 | 318±1.9<br>315.00±9.6<br>313±3.5$^{***b}$ | 310.1±1.8<br>311.5±9.9<br>306.5±9.1$^{***a***b}$ | 290.3±3.3<br>289.1±7.9<br>285.1±3.3$^{***a***b}$ | 280.00±2.4<br>275.6±6.5<br>270.00±6.3$^{***a***b}$ |
| DC2%Tween-80 | 327.1±6.4 | 328.66±9.8 | 328.21±4.2 | 329.1±5.3 | 329.4±2.3 |
| GLC5mg | 329.0±8.1 | 270.1±8.2$^{***a***b}$ | 185.5±2.1$^{***a***b}$ | 1777.6$^{***a***b}$ | 166±7.9$^{***a***b}$ |

**Note**: Each values represents mean ± SEM (n=6). a = compared to diabetes control; b = compared to baseline blood glucose level; **p<0.01, and ***p<0.001.
**Abbreviations**: *DP, Discopodium penninervum*; AF, aqueous fraction; CF, chloroform fraction; EF, Ethyl acetate fraction; DC, diabetes control; GLC, glibenclamide.

(P<0.001). In comparison to baseline time, no significant BGL reduction was detected in the 2% tween-80 and DW-treated group. At the 8th hour, the maximum percentage reduction in BGL was found in the EF 400mg, 46.7% in the DP400mg, and 49.5% in the GLC5mg-treated group compared to the respective baseline.

## The Effect of Repeated Daily Doses of Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* on Streptozocin-Induced Diabetic Mice

Normal and diabetic mice given DP, EF, DW10, and GLC5 after development of diabetes had their blood glucose levels tested once a week. Table 5 shows a summary of the findings. Diabetic mice revealed significant variations in blood glucose levels after induction compared to normal mice (p<0.001), but no differences in baseline fasting BGL across all diabetic mouse groups. At day zero, BGL was significantly different in streptozotocin-induced mice compared to normal controls (p<0.001). In addition to that, on the 7th and 14th days, when compared to diabetes control, the leaf extract and solvent fractions showed significant (p<0.01 and p<0.001) BGL reduction at all doses. Furthermore, at 14 days, the standard drug, GLC 5mg/kg exhibited a substantial (p<0.001) reduction in BGL compared to baseline. On the 7th and 14th days, however, the diabetes control and normal control groups demonstrated statistically negligible BGL reductions when compared to their respective baseline levels. The highest reduction in fasting BGL was achieved on the 14th day, with 47.9%, 46.8%, and 50.2%t for EF400, DP400, and GLC5mg, respectively.

## Effect of Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* on Body Weight of Streptozocin-Induced Diabetic Mice

Table 6 shows the body weight of diabetic and non-diabetic mice before and after the development of diabetes. The weight of mice was evaluated after 3 days of streptozotocin injection as a baseline, and there was no significant difference between diabetic groups, but there was a considerable weight loss when compared to the normal control group. When compared to the diabetic control, all doses of the leaf extract, standard medication, GLC 5mg, solvent fractions of ethyl acetate, and aqueous demonstrated significant (p<0.001) body weight improvement on day 14 of

**Table 5** The Effect of Repeated-Dose of Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* on Streptozocin-Induced Diabetic Mice

| Groups | Blood Glucose Level in mg/dl | | |
|---|---|---|---|
| | Day 0 | Day 7 | Day 14 |
| NC DW10ml<br>NC 2% T80 | 83.37±4.7***a<br>81.5±4.6***a | 82.8±3.00***a<br>80.2.±3.6***a | 84.33±8.8***a<br>80.1±6.1***a |
| DC DW10ml<br>DC 2% T80 | 335.5±1.8<br>327.1±6.4 | 341.2±8.2***b<br>331.5±5.1***b | 347.16±7.1***b<br>336.5±7.1***b |
| DP100mg<br>DP200mg<br>DP400mg | 330.3±2.1<br>320.8±1.16<br>323.7±2.3 | 193.22±5.4*a*c***b<br>200.6±3.2***a***b***c<br>189.00±4.2***a***b***c | 181±6.4***a***b***c<br>177.38±1.5***a***b***c<br>172.1±3.7***a***b***c |
| AF100mg<br>AF200mg<br>AF400mg | 328.31±8.8<br>334.4±7.5<br>331.00±6.4 | 208.00±2.1***a***b***c<br>213.00±4.8***a***b***c<br>2001.7±2.4***a***b***c | 203±5.5***a***b***c<br>194.33±4.5***a***b***c<br>173.0±2.26***a***b***c |
| EF100mg<br>EF200mg<br>EF400mg | 325.77±4.5<br>320.83±4.7<br>322.5±2.5 | 210.5±3.6*a*c<br>199.7±3.3**a***b***c<br>189.00±9.3***a***b***c | 185±6.3**a***c<br>182.8±4.2***a***b***c<br>168±4.7***a***b***c |
| GLC5mg | 329.0±8.1 | 180.00±8.3***a***b***c | 163.65±4.00***a***b***c |

**Notes**: Each values represent mean ± SEM (n = 6). DP = *Discopodium penninervum*; T80 = tween 80; a = compared to diabetes control; b = compare to normal control; c = compared to day zero (baseline blood glucose level); *p<0.05, **p<0.01, and ***p<0.001.
**Abbreviations**: AF, aqueous fraction; EF, ethyl acetate fraction; DC, diabetes control; GLC, glibenclamide; DW, distilled water; NC, normal control.

**Table 6** The Effect of Leaf Extract and Solvent Fractions of *Discopodium penninervum Hoschst* on Body Weight

| Groups | Body Weight of Mice in Gram | | |
|---|---|---|---|
| | Day 0 | Day 7 | Day 14 |
| NC DW10ml | 26.33±8.1 | 27.00±5.8*a | 27.66±5.5**a |
| NC 2% T80 | 26.65±4.8 | 27.00±7.3*a | 28.5±9.2**a |
| DCDW10ml | 28.64±5.7 | 23.5±4.3***b | 21.00±4.4***b |
| DC 2%T80 | 27.6±5.6 | 23.8±0.5.6***b | 22.66±6.2***b |
| DP100mg | 24.33±7.7 | 24.83±3.0***a | 25.16±2.7***a |
| DP200mg | 25.61±2.5 | 26.83±9.3***a | 28.0±6.5***a |
| DP400mg | 25.50±7.6 | 27.66±6.7***a | 29.16±4.50***a |
| AF100mg | 26.4±6.8 | 28.33±2.1***a | 28.7±7.5***a |
| AF200mg | 27.15±7.3 | 28.00±7.5***a | 30.33±3.6**a*b |
| AF400mg | 24.5±8.5 | 28.33±2.5***a | 31.1±5.2***a*b |
| EF100mg | 24.00±0. 57 | 28.16±3.0***a | 30.66±5.5***a |
| EF200mg | 25.5±3.9 | 27.51±2.1***a | 31.3±3.1***a |
| EF400mg | 27.33±2.8 | 30.65±5.9***a | 31.9±6.6*b***a |
| GLC 5mg | 27.33±2.7 | 31.5±5.3**a | 32±4.2***a |

**Notes**: Each values represents mean ± SEM (n = 6). a = compared to the diabetic control; b = compared to the normal control; T80 = tween 80 *p<0.05; **p<0.01, and ***p<0.001.
**Abbreviations**: DP, *Discopodium penninervum*; AF, aqueous fraction; EF, ethyl acetate fraction; DC, diabetes control; NC, normal control; GLC, glibenclamide; DW, distilled water.

treatment. In contrast, compared to the normal control group, the diabetic control group's body weight was considerably lower ($p<0.05$ and $p<0.001$) at the 7th and 14th days, respectively.

## The Effect of Leaf Extract and Solvent Fractions *Discopodium penninervum Hoschst* on Serum Lipid Profile of Streptozocin-Induced Diabetic Mice

In diabetic mice, there was a considerable increase in blood total cholesterol and triglycerides, as well as a significant decrease in HDL cholesterol, after induction of diabetes and subsequent treatment with leaf extract, solvent fractions, or glibenclamide, as shown in Tables 7 and 8. When compared to the diabetic control group, the aqueous fraction at doses of

**Table 7** The Effect of Leaf Extract and Aqueous Fractions of *Discopodium penninervum Hoschst* on Serum Lipid Profile of Diabetic Mice

| Groups | Effect of *Discopodium penninervum Hoschst* on Serum Lipid Profiles (mg/dl) | | | | |
|---|---|---|---|---|---|
| | STC | TG | LDL | VLDL | HDL |
| NC DW10ml | 87.30±4.1***a<br>179.1±2.5***b | 78.3±3.1***a<br>174±4.5***b | 33.2±5.1***a<br>128.1±2.4***b | 19.1±3.7***a<br>31.2±2.5***b | 36.1±8.7***a<br>21.5±3.1***b |
| DP100mg | 168.4±5.6***a***b | 148.9±2.8***a***b | 110.1±8.7***a***b | 28.2±4.2***a***b | 31.8±1.5***a***b |
| DP200mg | 162.66±1.3***a***b | 141.22±1.5***a***b | 103.50±1.50***a***b | 25.66±4.3***a***b | 32.50±2.7***a |
| DP400mg | 160.7±2.67***a***b | 139.15±3.5***a***b | 101.00±2.3***a***b | 24.6±4.6***a***b | 34.7±1.8***a |
| AF100mg | 171.66±2.7***a***b | 173.7±2.6***b | 114.50±2.4***a***b | 33.33±8.3***b | 25.16±2.7***b |
| AF200mg | 166.65±1.76***a***b | 155.76±3.5***a***b | 110.66±1.98***a***b | 29.12±1.16***b | 26.83±1.24*a***b |
| AF400mg | 160.66±5.6***a***b | 148.33±3.6***a***b | 104.16±3.8***a***b | 27.33±3.5*a***b | 28.9±4.1*a***b |
| GLC 5mg | 97.33±1.13***a | 84.22±7.4***a***b | 38.16±6.5***a | 18.9±0.9***a | 37.16±5.8***a |

**Notes**: Each values represents mean ± SEM (n=6). a = compared with diabetic control, b= compared with normal control group, *p < 0.05, **p < 0.01, ***p < 0.001.
**Abbreviations**: GLC, glibenclamide; DC, diabetic control; NC, normal control; STC, serum total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; VLDL-c, very-low-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; DP, *Discopodium penninervum*; AF, aqueous fraction; GL, glibenclamide; DW, distilled water.

**Table 8** Effect of Ethyl Acetate Fraction of *Discopodium penninervum Hoschst* on Serum Lipid Profile of Diabetic Mice

| Groups | Effect of *Discopodium penninervum Hoschst* on Serum Lipid Profiles (mg/dl) | | | | |
|---|---|---|---|---|---|
| | STC | TG | LDL | VLDL | HDL |
| NC 2%T80 | 83.00±0.77***a | 76.5±0.68***a | 32.16±0.66***a | 16.43±1.6***a | 35.00±1.23***a |
| DC2%T 80 | 183.23±1.7***b | 172.5±1.99***b | 125.66±1.55***b | 32.83±1.9***b | 25.11±0.33***b |
| EF100mg | 173.32±1.47***a***b | 141.46±4.2***a***b | 113.77±2.7***a***b | 28.5±4.1***a***b | 33.33±5.5***a |
| EF200mg | 164.42±1.3***a***b | 139.83±0.34***a***b | 105.21±2.5***a***b | 26.16±3.5***a***b | 37.33±3.3***a |
| EF400mg | 157.24±2.2***a***b | 130.05±2.6***a***b | 94.16±3.37***a***b | 28.00±7.55***a***b | 38.83±8.3***a |
| GLC5mg | 92.31±1.4***a***b | 79.44±5.5***a***b | 36.16±2.4***a | 20.01±0.55***a | 39.16±2.67***a***b |

**Notes**: Each values represents mean ± SEM (n=6). a = compared to diabetes control, b = compared to normal control. *p<0.05, **p<0.01 and ***p<0.001.
**Abbreviations**: GLC, glibenclamide; EF, ethyl acetate fraction; DC, diabetic control; NC, normal control; 2%T 80, two percent tween eighteen; STC, serum total cholesterol; TG, Triglyceride; HDL-c, high-density lipoprotein cholesterol; VLDL-c, very-low-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol.

100 mg/kg and 200 mg/kg, the ethyl acetate fraction (100 mg/kg), and the leaf extract all demonstrated negligible reductions in STC and LDL. However, when diabetic mice were given all two doses of leaf extract (DP200 and DP400), ethyl acetate fraction (EF 200 and 400), aqueous fraction (AF400), and GLC5mg for 14 days, there was a significant ($p<0.001$) dose-dependent reduction in the serum levels of TC, STG, TG, LDL, and VLDL while increasing the levels of HDL.

## Antioxidant Activity of Leaf Extract of *Discopodium penninervum Hoschst in* Diphenyl-2-Picrylhydrazyl Assay

The lowest anti-oxidant activity was achieved at the lowest test concentration (15.625g/mL), while the highest anti-oxidant activity was obtained at the highest test concentration (500 g/mL) for leaf extract of *Discopodium penninervum Hoschst* and the standard medication, ascorbic acid. Ascorbic acid-like antioxidant activity of the leaf extract was boosted in a concentration-dependent or dose-dependent manner (Table 9).

**Table 9** Antioxidant Activities of the Crude Leaf Extract of *Discopodium penninervum Hoschst* in Diphenyl-2-Picrylhydrazyl Assay

| Concentration (µg/mL) | % Inhibition of DPPH | |
|---|---|---|
| | Leaf Extract | Ascorbic Acid |
| 15.625 | 3.1±0.4 | 13.2±0.1 |
| 31.25 | 4.4±0.19 | 27.01±0.5 |
| 62 | 9.11±0.51 | 48.15±0.34 |
| 125 | 18.5±0.66 | 56.45±0.67 |
| 250 | 28.4±0.31 | 68.3±0.23 |
| 500 | 45.31±0.23 | 83.55±011 |
| IC50 | 10.23±0.45 | 4.1±0.88 |

**Notes**: Each value of % inhibition of DPPH free radical is presented as mean ± SEM, n = 3.
**Abbreviations**: DPPH, 2,2-diphenyl-1-picrylhydrazine; IC50, half-maximal inhibitory concentration; SEM, standard error of mean.

## Discussion

Diabetes is one of the most common chronic diseases, and it is linked to hyperlipidemia as well as comorbidities including obesity and hypertension. As a result, promising plant-derived antidiabetic molecules that can act on various disease-related pharmacological targets and have been shown to be safe over time are currently needed for the treatment of diabetes. Flavonoids, phenolic compounds, alkaloids, terpenoids, saponins, tannins, glycosides, glycolipids, dietary fibers, and carotenoids have all been found to have powerful anti-diabetic effects.[37] The goal of this study was to test the in vivo antidiabetic, anti-hyperlipidemia, and in vitro antioxidant activity of *Discopodium penninervum Hoschst* leaf extract and solvent fractions on normal, oral glucose- loaded, and diabetic mice in order to validate its traditional use in the treatment of DM in humans. The leaf extract was deemed to be safe at a dose of 2000 mg/kg since no signs of acute toxicity were observed in leaf extract-fed female mice over the 2-week observation period, as established by OECD guidelines. This indicates that the LD50 of *Discopodium penninervum Hoschst* Hydromethanolic Leaf Extract is >2 g/kg. Based on the results of the acute toxicity test, dosages of Hydromethanolic leaf extract of 100, 200, and 400 mg/kg were chosen for hypoglycemia and antihyperglycemic investigations 2008:425.[38,39] Streptozotocin was employed to produce diabetes in the current investigation. The streptozotocin-induced animal model can be explained as a useful tool for studying the effects of anti-diabetic drugs like glibenclamide on DM. By destroying pancreatic cells, STZ is known to cause diabetes, hyperinsulinemia, and hyperglycemia. The 80% methanolic leaf extract of *Discopodium penninervum Hoschst* at all three doses, as well as glibenclamide at a dose of 5 mg/kg, demonstrated considerable hypoglycemic action in normoglycemic mice. Because glibenclamide stimulates insulin release from pancreatic cells while inhibiting glucagon secretion, it has a hypoglycemic effect.[40] It is possible that the leaf extract has an insulin-like effect or stimulates insulin secretion in cells. Flavonoids and tannins derived from medicinal plants have been shown to enhance insulin production from pancreatic cells.[41] Because these active ingredients are found in *Discopodium penninervum Hoschst*, the plant leaf extract's mode of action is likely to be comparable to that of glibenclamide.

In the current investigation, oral administration of *Discopodium penninervum Hoschst* to glucose-challenged mice at all tested dosages (100mg/kg, 200mg/kg, and 400mg/kg) resulted in a significant ($p< 0.001$) decline in blood glucose level within 60 minutes after treatment when compared to the negative control. Similarly, from 30 minutes onwards, GLC 5mg/kg demonstrated a considerable drop in blood glucose levels. This suggests that the leaf extract can effectively reduce increased blood glucose levels, implying that it may have a role in reducing postprandial hyperglycemia and DM complications. Flavonoids have been shown to help people with diabetes mellitus either by preventing glucose absorption (by inhibiting -glycosidase activity in the intestine) or by improving glucose tolerance.[42] This could be one of *Discopodium penninervum Hoschst* extract's strategies for improving glucose tolerance. Because this active constituent existed in *Discopodium penninervum Hoschst*, the results of the in vitro DPPH scavenging experiment revealed that the dosage dependent radical scavenging activity of *Discopodium penninervum Hoschst* could be a probable mechanism of antihyperglycemic action of the extract. Plants with high levels of phytochemicals, such as phenolic and flavonoid components, have powerful antioxidant capabilities.[43] The presence of flavonoid compounds in *Discopodium penninervum Hoschst* extract may explain its antioxidant properties and flavonoid compounds have the ability to donate hydrogen atoms or electrons and therefore capture free radicals.[44] In single dose, when compared to baseline and diabetic control data, the chloroform fraction showed a significant ($p<0.001$) BGL reduction after 8 hours of therapy in the single-dose diabetic animal at a dose of 400mg/kg. The chloroform fraction, on the other hand, demonstrated statistically insignificant BGL reduction when compared to baseline blood glucose levels at doses of 100mg/kg and 200mg/kg. This could be attributed to a lack of active metabolite (s) concentrations in the lower doses of 100 mg/kg and 200 mg/kg, compared to the maximum dose of 400 mg/kg. Furthermore, when compared to leaf extract and other fractions such as ethyl acetate and aqueous fractions, the chloroform fraction had low BGL reduction activity.[40] Furthermore, the presence of less secondary metabolites in the chloroform fraction compared to the other fractions and leaf extract of *Discopodium penninervum Hoschst* could be a factor and the chloroform fraction was not further examined for its in vivo antihyperglycemic effect of repeated daily dosing on diabetic mice since it showed less reduction in BGL. The solvent fractions and the standard medication have showed a considerable reduction in fasting blood glucose levels when compared to the diabetic control group in repeated daily doses. Again, at the 14th day, all doses of the solvent fractions for the aqueous fraction and ethyl acetate fraction

(100mg/kg, 200mg/kg, and 400mg/kg) induced a maximum decline in fasting BGL of 47.9%, 46.8%, and 40%, respectively. Excessive free radicals produced by hyperglycemia-induced glucose autoxidation and protein glycosylation are critical in the pathophysiology of diabetes,[45,46] and.[47] Previous research has shown that several plant extracts have pancreas cell-protective effect due to their antioxidant activities[48] and this could be the method through which *Discopodium penninervum Hoschst* lowers blood glucose levels because it has established antioxidant activity. STZ-induced diabetes is characterized by rapid weight loss and mice with acute hyperglycemia lose a significant amount of weight after being treated with STZ. Similarly, in this study, STZ induced considerable body weight loss in diabetic control mice in the current investigation. STZ induces hyperglycemia, which results in weight loss due to increased squandering of fat stores, muscle, and tissue proteins. As a result, weight increase in STZ-induced diabetic mice after repeated treatment of the hydromethanolic *Discopodium penninervum Hoschst* leaf extract reveals that the extract has antihyperglycemic potential.[49,50] Insulin shortage causes lipoprotein lipase activity to diminish, resulting in lower clearance of VLDL and chylomicrons in the body.[22] The serum lipid profile of STZ-induced diabetic control mice was dramatically raised in this study, including STC, STG, VLDL-C, and LDL-C, whereas HDL-cholesterol was lowered, as expected. In a dose-dependent manner, administration of *Discopodium penninervum Hoschst* leaf extract and the solvent fraction for 2 weeks lowered serum STC, STG, VLDL-C, and LDL-C while increasing HDL-C. It is unclear whether *Discopodium penninervum Hoschst* has a direct influence on lipid metabolism or whether the antidyslipidemic efficacy is solely related to reduced hyperglycemia. However, it is possible to conclude that *Discopodium penninervum Hoschst* improves diabetic dyslipidemia. In addition to that, the plant extract and solvent fraction may also have a direct effect on glucose utilization in diabetic mice, and the plant extract and solvent fraction may have a direct influence on glucose utilization in diabetic mice.[51]

## Conclusion

The 80% methanolic leaf extract, aqueous fraction, and ethyl acetate fractions of *Discopodium penninervum Hoschst* showed significant blood glucose level reduction in diabetic, normoglycemic, and oral glucose loaded mice, as well as body weight gain in diabetic mice, according to this study. The chloroform fraction also had a low blood glucose reduction in streptozotocin-induced mice, according to the findings.

The findings further confirmed that the extract's free radical scavenging activity may contribute to its antihyperglycemic and antihyperlipidemic properties.

## Abbreviations

ANOVA, analysis of variance; BGL, blood glucose level; DPPH, diphenyl-1-picrylhydrazyl; DM, diabetes mellitus; FPG, fasting plasma glucose; IDF, International Diabetes Federation.

## Data Sharing Statement

On reasonable request, the corresponding author will provide the datasets used and/or analyzed during the current work.

## Ethical Approval

The ethical review committee of Mettu University's Pharmacy Department authorized the experiment protocol with MeU/111/508 ethical approval number.

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## Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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