World Journal of Current Medical and Pharmaceutical Research
Content available at www.saap.org.in ISSN: 2582-0222

EVALUATION OF THE ANTIDIABETIC AND ANTIOXIDANT PROPERTIES OF SNEHAKANTHI: A LICENSED POLYHERBAL FORMULATION IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

BADMANABAN R[1], ELAYATH PARVATHY MURALI[2*], BRAHMADATHAN U[3]

[1]Principal and Professor, Nirmala College of Pharmacy, Muvattupuzha P.O., Ernakulam dist., Kerala-686661, affiliated to Kerala University of Health Sciences, Thrissur, Kerala.

[2*]Associate Professor, Department of Pharmacology, Nirmala College of Pharmacy, Muvattupuzha P.O., Ernakulam dist., Kerala-686661, affiliated to Kerala University of Health Sciences, Thrissur ,Kerala.

[3]Additional Medical Officer (Production - Siddha), Santhigiri Ayurveda & Siddha Vaidyasala, Additional Charge - Santhigiri Scientific and Industrial Research Institute, Santhigiri Ashram, Santhigiri P. O, Thiruvananthapuram, Kerala, 695589

ARTICLE HISTORY

Received on: 14-06-2026
Revised on: 03-07-2026
Accepted on: 28-08-2026

ABSTRACT

The present study was undertaken to evaluate the antidiabetic and antioxidant effects of Snehakanthi, a proprietary polyherbal formulation containing *Salacia reticulata*, *Trigonella foenum-graecum*, *Tribulus terrestris*, *Strychnos potatorum* and *Phyllanthus emblica*, in streptozotocin (STZ)-induced diabetic rats. The acute oral toxicity of Snehakanthi was initially evaluated, following which its antidiabetic activity was assessed at doses of 200 and 400 mg/kg for 28 days. Fasting blood glucose (FBG), oral glucose tolerance and body weight were evaluated, while tissue antioxidant status was assessed by estimating superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and reduced glutathione (GSH) levels in the liver, kidney and pancreas. Histopathological examination of the liver and pancreas was also performed. Snehakanthi was well tolerated up to 2000 mg/kg, with no mortality or apparent signs of toxicity. Treatment with Snehakanthi improved glycaemic parameters, with more pronounced effects at 400 mg/kg. The 400 mg/kg dose significantly reduced FBG ($p<0.0001$) on day 28 and significantly improved glucose tolerance at 60, 90 and 120 min ($p<0.0001$) compared with diabetic control. It also significantly attenuated diabetes-associated body weight loss ($p<0.0001$). Furthermore, Snehakanthi at 400 mg/kg significantly improved SOD, CAT, GPx and GSH levels in several tissues, particularly the liver and pancreas, compared with diabetic control. Histopathological examination revealed comparatively preserved hepatic and pancreatic architecture in Snehakanthi-treated animals. Overall, Snehakanthi demonstrated significant antihyperglycaemic and antioxidant effects in STZ-induced diabetic rats, accompanied by attenuation of diabetes-associated hepatic and pancreatic histopathological alterations. These findings suggest that the beneficial effects of Snehakanthi may be associated with improved glycaemic control and attenuation of diabetes-induced oxidative stress, supporting its potential as a polyherbal intervention for experimental diabetes.

Keywords: *Antidiabetic, Snehakanthi, Polyherbal, Antioxidant, Streptozotocin, Wistar rats.*

***Corresponding Author**
Elayath Parvathy Murali

DOI: https://doi.org/10.37022/wjcmpr.v8i2.418

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both, leading to disturbances in carbohydrate, protein and lipid metabolism. If inadequately controlled, diabetes may result in acute metabolic complications such as diabetic ketoacidosis and hyperosmolar hyperglycaemic state, as well as long-term microvascular and macrovascular complications including nephropathy, retinopathy, neuropathy, cardiovascular disease, stroke and diabetic foot ulcers [1]. According to the International Diabetes Federation, approximately 537 million adults aged 20–79 years were living with diabetes in 2021, corresponding to a global prevalence of approximately 10.5% in this age group [2]. Type 2 diabetes mellitus accounts for the vast majority of diabetes cases worldwide.

Type 1 diabetes: Type 1 diabetes is primarily caused by autoimmune destruction of pancreatic β-cells, resulting in an absolute deficiency of insulin. Although it commonly manifests in children and young adults, it can occur at any age [3,4].

Type 2 diabetes: Type 2 diabetes is the most common form of diabetes, accounting for approximately 90–95% of cases. It is characterized by insulin resistance accompanied by a progressive inability of pancreatic β-cells to secrete sufficient insulin, resulting in relative insulin deficiency. Although it is more common in adults, type 2 diabetes can occur in children and adolescents, particularly in populations at increased risk [3,4].

Gestational diabetes mellitus (GDM) is characterized by hyperglycaemia first detected during pregnancy. Globally, approximately one in 25 pregnancies is affected by GDM, which is associated with adverse maternal and fetal outcomes during the perinatal period and an increased risk of type 2 diabetes in later life [5].

Clinical manifestations of diabetes mellitus commonly include polyuria, polydipsia, polyphagia, unexplained weight loss, fatigue, blurred vision, irritability or mood changes, dry or itchy skin, and delayed healing of cuts and wounds. The onset and progression of symptoms vary according to the type of diabetes. In type 1 diabetes, symptoms may develop rapidly over a period of a few weeks to months and may be severe, whereas symptoms of type 2 diabetes generally develop more gradually over several years and may remain unrecognized for a prolonged period [6].

Medicinal plants and their bioactive constituents have been traditionally used in many healthcare systems worldwide, including for the management of diabetes mellitus. Several medicinal plants with reported antidiabetic properties have been investigated as potential therapeutic agents or as sources of bioactive compounds and functional food supplements that may complement conventional diabetes management [7].

The polyherbal formulation under study – **Snehakanthi**, is a licensed proprietary formulation developed and manufactured by Santhigiri Ayurveda and Siddha Vaidyasala**.** The formulation used in the present study was provided through Navajyothi Sree Karunakara Guru Research Centre for Ayurveda and Siddha. It consists of powdered plant parts derived from Salacia reticulata, Trigonella foenum-graecum, Tribulus terrestris, Strychnos potatorum and Phyllanthus emblica. The individual plant constituents of the formulation have been reported to exhibit diverse pharmacological activities, including antioxidant, anti-inflammatory, analgesic/ antinociceptive, antimicrobial, antibacterial and antipyretic effects.[8,9,10] Phytoconstituents reported in the constituent plants of Snehakanthi, including gallic acid, quercetin, ellagic acid and epicatechin, have been associated with modulation of oxidative stress and inflammatory signalling pathways, including NF-κB and PPAR-γ [11,12,13]. The purpose of this study was to assess the in vivo antidiabetic and antioxidant properties of Snehakanthi formulation.

METHODOLOGY

PREPARATION OF TEST SUSPENSION: Snehakanthi is a licensed proprietary formulation developed and manufactured by Santhigiri Ayurveda and Siddha Vaidyasala (Mfg.Lic.No: 61/25D/9). The test samples were collected from Batch no: SP179 (Mfg.date: 11/2022). Each capsule of 500mg consists of 99.5 mg of powdered plant parts of Salacia reticulata, Trigonella foenum-graecum, Tribulus terrestris, Strychnos potatorum and Phyllanthus emblica each and also contains excipients like starch IP (1mg), sodium benzoate IP (0.7mg) and colloidal silicon dioxide IP (0.8mg). It was prepared as suspension using 0.5% carboxy methylcellulose (CMC).

IAEC APPROVAL

The laboratory animals used in this experimental study got the approval from the Institutional Animal Ethics Committee of Nirmala College of Pharmacy (Registration no: 1411/PO/Re/S/11/CPCSEA). Details of project proposal sanctioned by IAEC are as follows:

Project proposal no. : NCP/IAEC/2022/Protocol VII

Approved protocol title: Evaluation of antidiabetic activity of polyherbal formulation

Approved date: 17/12/2022

Animals used: 39 Wistar rats (age: 60-80 days)(9 female rats-acute toxicity studies, 30 male rats-antidiabetic studies)

ACUTE TOXICITY STUDY

For acute toxicity studies 9 female Wistar albino rats were required as per OECD guideline 423. In accordance with annex 2c of OECD guideline 423 (Acute toxic class method), which suggests a starting dose of 300 mg/kg body weight for the extract whose toxicity is unknown, the rats were divided into cages and placed in groups of three. It indicates that the next larger dose (2000 mg/kg body weight) should be used if two-thirds of the animals survive after the dose is administered. If two-thirds of the animals survive after receiving 2000 mg/kg, the same dosage will be administered for confirmation. [14]

IN VIVO ANTIDIABETIC STUDIES

Experimental Animals

Wistar albino rats (180-220g) were purchased from disease free animal house of Vaarunya Biolabs Private Limited Bengaluru, Karnataka (Reg.no: 2076 / PO / RcBiBt /S /19 /CPCSEA). The animals were kept in separate groups in a laboratory setting with free access to food and water, at room temperature between 22 and 24°C, and in alternate light and dark cycles lasting 12 hours each. The antidiabetic study, which took place between 9:00 and 17:00, required the animals to acclimatise for 14 days.

Experimental design

Table 01: Induction of diabetes in rats

Sl. No	Group	Treatment	Route of administration
1	Group I Normal Control	Vehicle (0.5% CMC)	p.o.
2	Group II Diabetic control	Streptozotocin (60 mg/kg)	i.p.
3	Group III Standard group	Streptozotocin (60 mg/kg) + Glibenclamide (10 mg/kg)	i.p. + p.o.
4	Group IV Treatment group	Streptozotocin (60 mg/kg) + Snehakanthi formulation (low dose)	i.p. + p.o.
5	Group V Treatment group	Streptozotocin (60 mg/kg) + Snehakanthi formulation (high dose)	i.p. + p.o.

Induction of diabetes in rats

The rats were allowed to fast overnight following 14 days of acclimation. An intraperitoneal injection of 60 mg/kg streptozotocin, freshly dissolved in 0.1M citrate buffer pH 4.5, was used to induce diabetes (as shown in figure 1). To minimize acute STZ-induced hypoglycemia, a 5% glucose solution was administered to the animals overnight and they were allowed to consume water. Animals having blood glucose levels more than 250 mg/dl were deemed diabetic and included in the experiment after their levels were tested 72 hours later.[15] On the third day following the streptozotocin injection, the plant extract was administered (as shown in figure 2); this is regarded as the first day of therapy, which lasted for 28 days. [16]

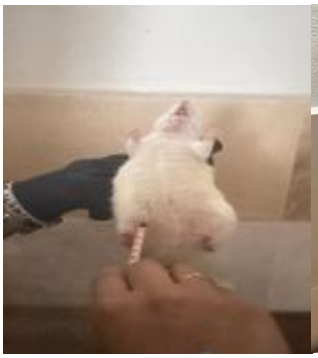

Figure 01: Induction of diabetes in rats

Figure 2: Administration of drug in rats

30 rats were randomly divided into different groups including normal control group, diabetic control group, standard group (Glibenclamide10mg/kg) and treatment group (high dose and low dose). Test group of animals were treated with low dose (200mg/kg) and high dose (400mg/kg) of Snehakanthi formulation (which was prepared in 0.5% CMC) and standard group Glibenclamide (10mg/kg) (prepared in 0.5% CMC) by oral administration. The drug administration was continued for 28 days, given once daily [17].

Fasting blood glucose levels and body weight were assessed on days 0, 7, 14, 21, and 28. FBG was determined using a one-touch glucometer using blood obtained from the tail vein. An oral glucose tolerance test (OGTT) was also performed to evaluate glucose handling following an oral glucose challenge, with blood glucose levels measured at predetermined intervals after glucose administration [18].

BIOCHEMICAL PARAMETERS

Estimation of blood glucose levels

a) Fasting blood glucose (FBG) test

Diabetes mellitus severity is directly correlated with fasting glucose levels. The rats were fasted for at least eight hours, generally in the morning, before blood was obtained from the tip of the tail vein by snipping the tail. The one-touch glucometer was used for this. The fasting glucose test was conducted on days 0, 7, 14, 21, and 28 in order to validate the findings.[18]

b) Oral glucose tolerance test (OGTT)

Rats in all experimental groups were administered glucose orally at a dose of 2 g/kg, one hour following administration of the respective treatments. At 0, 30, 60, 90, and 120 minutes, blood samples were taken via tail snip. The blood glucose level was calculated at periodic time intervals using one-touch glucometer [18].

c) Body weight comparison test

On days 0, 7, 14, 21, and 28, the rats' body weight was recorded. After diabetes was induced, the rats' body weights decreased, as seen by a comparison between the diabetic rats and the normal control group [18].

HISTOPATHOLOGICAL EXAMINATION

Following the conclusion of the study, the euthanization of animals was done using a CO_2 chamber. After being cleaned with ice-cold 0.9% saline, the liver and pancreas were preserved in 10% formalin embedded in paraffin and then sliced into sections that were 5 µm thick using a microtome. Standard procedures were used to mount the sections on glass slides. Following hematoxylin-eosin staining, the sections were seen at 40X magnification and captured on camera using a light microscope [19].

ANTIOXIDANT TESTS USING BIOMARKERS

Following the conclusion of the study, the euthanization of animals was done using a CO_2 chamber, and their pancreas, liver, and kidney were removed. Within 30 minutes following dissection, the liver, kidneys, and pancreas were further processed, weighed, and kept on ice after being cleaned with ice-cold phosphate buffer. On the same day, oxidative stress was estimated. Ten times (w/v) sodium phosphate buffer pH 7.8 was used to homogenize the tissue from the liver, kidney, and pancreas. The supernatant was utilized to estimate the levels of glutathione peroxidase (GPX), reduced glutathione (GSH), catalase, and superoxide dismutase (SOD) after the homogenate was centrifuged for 15 minutes at 3000 rpm in a tabletop centrifugal machine.

a) Estimation of Superoxide dismutase (SOD)

50µl of tissue samples were added to the reaction mixture containing 50mM phosphate buffer (pH 7.8), 45µM methionine, 5.3mM riboflavin and 84µM potassium ferric cyanide. The tubes were then incubated at 25°C for 10 minutes and the absorbance was read on spectrophotometer at 600nm [20].

b) Estimation of Catalase (CAT)

To 1.2 ml of 0.01Mm phosphate buffer (pH 7.0), 0.5ml of tissue homogenate was added. The enzyme reaction was started by the addition of 1 ml of 0.2mM hydrogen peroxide solution. The decrease in absorbance was measured at 240nm for every 30 seconds up to3 minutes. The enzyme blank was run simultaneously with 1 mlof distilled water instead of hydrogen peroxide. The enzyme activity was expressed as enzyme unit /mg of protein [21].

c) Estimation of Reduced Glutathione (GSH)

1ml of tissue homogenized in PBS was taken in a test tube. 0.5mL of phosphate buffer (0.2M pH 8), 1.3mL distilled water and 0.2mL of DTNB (0.6mM) were added. The contents were mixed well and read on spectrophotometer at 420nm. The GSH levels were compared with a standard reduced glutathione graph. [22]

d) Estimation of Glutathione Peroxidase (GPx)

50µl of tissue homogenate was added to a test tube containing 3ml of reaction mixture [1mg of β -NADPH +1mM glutathione reduced]. Mixed by inversion and equilibriated to 25°C and monitored the absorbance at 340nm until constant. The tube

containing 3ml reaction mixture and 50µl of phosphate buffer with Dithiothreitol at pH 7 was taken as blank. 50µl of 0.042% hydrogen peroxide was added to these tubes. Immediately mixed by inversion and recorded the decrease in absorbance at 340nm for approximately 5 minutes [23].

STATISTICAL ANALYSIS

The statistical analysis was performed using GraphPad Prism Version 9.5. All the results were expressed as Mean ± SEM. The data were analysed using Two way Analysis of Variance (ANOVA) followed by Dunnett's multiple comparison test.

RESULTS

ACUTE TOXICITY STUDY

Determining a drug's therapeutic index and confirming its safety in vivo are the goals of acute toxicity studies. The acute toxic class method (OECD 423) help in an approximate assessment of LD50 value in experimental animals. The acute oral toxicity studies of the Snehakanthi formulation were studied on female Wistar rats as per OECD guidelines 423 of acute toxic class method. Up to the dosage level of 2000 mg/kg, there was no fatality, according to the OECD guidelines 423 of acute toxic class method. At the conclusion of the 14-day observation period, all the animals were observed to be normal and had no noticeable behavioral changes. The animals were sacrificed and organs isolated indicated no gross morphological changes as well. (as shown in figures 3, 4, 5 and 6)

The rats tolerated the dose up to 2000 mg/kg well, and there were no appreciable differences in body weights before and after the treatment period. Therefore 200mg/kg (1/10th of the maximum safe tolerable dose of the extract) and 400mg/kg (1/5th of the maximum safe tolerable dose of the extract) were selected for evaluation of in vivo antidiabetic activity.

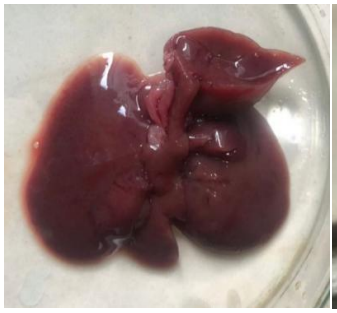

Figure 03: Liver

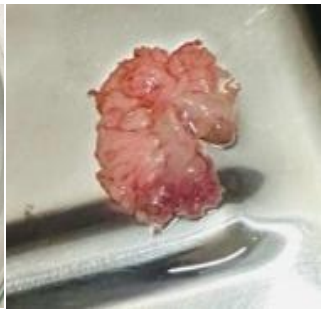

Figure 04: Pancreas

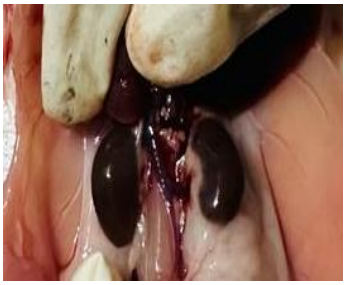

Figure 05: Kidneys

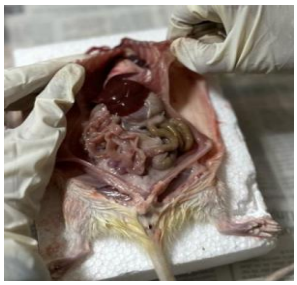

Figure 06: Organ system

BIOCHEMICAL PARAMETERS

Effect of Snehakanthi formulation on Fasting Blood Glucose (FBG) levels

On days 0, 7, 14, 21, and 28 of drug administration, the fasting blood glucose levels of both normal and experimental rats were assessed in comparison to diabetic control group. It was observed that there was a **progressive increase in fasting blood glucose (FBG) in the diabetic control group**, while in contrast, both **glibenclamide and Snehakanthi produced progressive reductions in FBG throughout the 28-day treatment period**. On day 28, **Snehakanthi (400 mg/kg) exhibited a highly significant reduction (p<0.0001) in FBG compared with the diabetic control group.** The 200 mg/kg dose also produced a significant reduction on day 28 (p<0.0001). The findings indicate a **dose-dependent anti-hyperglycaemic effect of Snehakanthi.** (as shown in table 02 and figure 07).

Table 02: Fasting blood glucose levels

Groups	Day 0	Day 7	Day 14	Day 21	Day 28
Group 1 Normal control	81.16 ±1.16	82.16±0.90	83.33±1.35	82.66±1.14	82.16±0.79
Group 2 Diabetic control	314± 1.63	328±1.36	341.33±2.02	369.83±2.78	382.16±0.83
Group 3 STZ + GBC (10 mg/kg)	293± 2.03*	213±1.46***	151±2.38****	125.16±1.42****	101.67±0.88****
Group 4 STZ + SKF (200 mg/kg)	303± 1.82*	299.33± 1.35*	229.83±1.4**	169.33±2.54****	148±1.36****
Group 5 STZ + SKF (400 mg/kg)	300± 1.57*	264±1.52**	169.83±1.57****	138.16±1.19****	104.5±1.68****

Values are given as mean ± SEM (n=6).

*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 when compared to Diabetic control group (two-way ANOVA followed by Dunnett test) (SKF- Snehakanthi formulation)

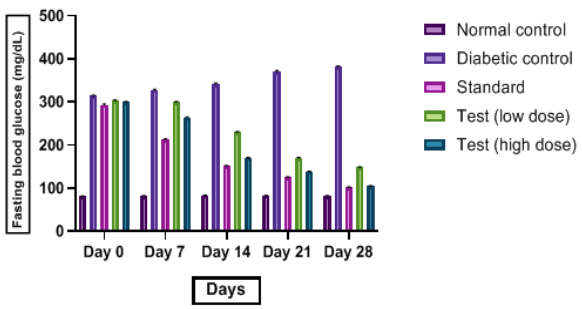

Figure 07: Fasting blood glucose level

Effect of Snehakanthi formulation on Oral glucose tolerance tests (OGTT)

The OGTT results show that the diabetic control group had markedly elevated blood glucose throughout the 120-minute period, with a peak at 30th minute and only a gradual decline thereafter. In contrast, both glibenclamide and Snehakanthi markedly improved glucose tolerance. **Snehakanthi 400 mg/kg significantly reduced blood glucose at 0, 30, 60, 90 and 120 min compared with the diabetic control group (p<0.0001 at all time points).** The 400 mg/kg dose showed a greater improvement than the 200 mg/kg dose and produced a response comparable to glibenclamide, indicating a **pronounced antihyperglycaemic and glucose-tolerance-improving effect of Snehakanthi.** (as shown in table 03and figure 08)

Table 03: Oral glucose tolerance test

Groups	0 min	30 min	60 min	90 min	120 min
Group 1 – Normal control	82.16 ± 0.79	169.32 ± 1.39	158.22 ± 1.80	141.00 ± 1.10	128.13 ± 1.01
Group 2 – Diabetic control	382.16 ± 0.83	499.63 ± 1.78	455.14 ± 1.12	410.09 ± 1.49	400.15 ± 1.81
Group 3 – STZ + GBC (10 mg/kg)	101.67 ± 0.88****	187.42 ± 0.95****	122.18 ± 1.10****	110.54 ± 0.96****	98.27 ± 0.88****
Group 4 – STZ + SKF (200 mg/kg)	148.00 ± 1.36****	228.12 ± 1.35****	165.27 ± 1.81****	152.25 ± 1.01****	140.49 ± 0.76****
Group 5 – STZ + SKF (400 mg/kg)	104.50 ± 1.68****	191.34 ± 1.58****	126.80 ± 1.68****	116.24 ± 0.98****	108.63 ± 0.88****

Values are given as mean ± SEM (n=6).

*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 when compared to Diabetic control group (two-way ANOVA followed by Dunnett test)

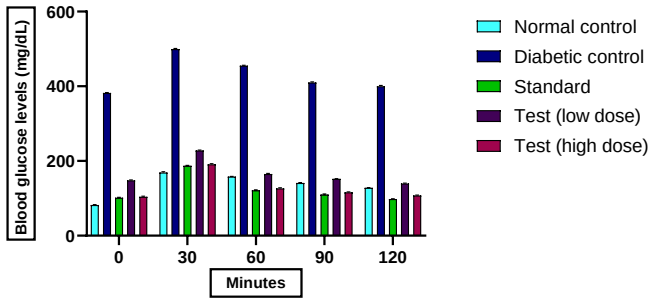

Figure 08: Oral glucose tolerance test

Effect of Snehakanthi formulation on body weight (BW)

The diabetic control group showed a progressive decline in body weight fromday 0 today 28, indicating diabetes-associated weight loss. In contrast, both glibenclamide and Snehakanthi treatment attenuated this decline. **Snehakanthi (400 mg/kg) significantly improved body weight from day 14 onwards**. On 28th day, it was observed that rats treated with a high dose of SKF (400 mg/kg) had a statistically significant (p<0.0001) increase in body weight compared to rats of diabetic control group. The 200 mg/kg dose showed a similar but somewhat lesser effect. Overall, the findings indicate that Snehakanthi, particularly at **400 mg/kg, significantly attenuated diabetes-associated body-weight loss** over the 28-day treatment period. (as shown in table 03 and figure 09)

Table 04: Body weight comparison

Groups	Day 0	Day 7	Day 14	Day 21	Day 28
Group 1 – Normal control	188.12 ± 1.30	191.26 ± 2.67	195.42 ± 0.89	200.37 ± 1.39	210.17 ± 0.76
Group 2 – Diabetic control	182.32 ± 2.45	155.56 ± 1.43	148.65 ± 1.17	139.18 ± 2.23	130.32 ± 1.28
Group 3 – STZ + GBC (10 mg/kg)	190.21 ± 1.81	159.47 ± 2.27*	167.24 ± 1.48***	175.34 ± 0.78****	185.27 ± 2.56****
Group 4 – STZ + SKF (200 mg/kg)	182.18 ± 2.45	158.13 ± 0.87*	164.28 ± 2.32**	165.16 ± 0.86***	169.28 ± 1.16****
Group 5 – STZ + SKF (400 mg/kg)	187.36 ± 2.78	161.32 ± 1.65*	168.36 ± 2.67***	171.23 ± 1.06****	179.22 ± 2.24****

Values are given as mean ± SEM (n=6).

*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 when compared to Diabetic control group (two-way ANOVA followed by Dunnett test).

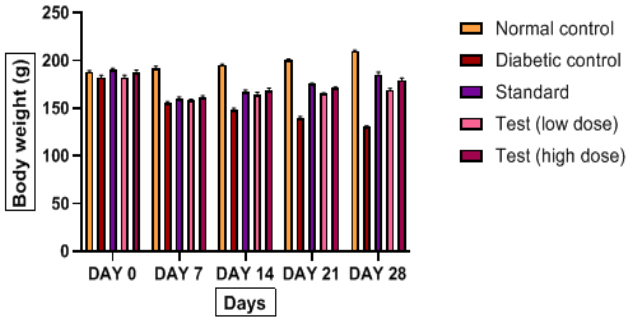

Figure 09: Body weight comparison

Histopathological Studies

All the animals were sacrificed at the conclusion of the 28th day in order to obtain the liver and pancreas. After being cleaned in ice-cold 0.9% saline, the organs were preserved in 10% formalin embedded in paraffin and then sliced into sections that were 5 µm thick using a microtome. Standard methods were used to mount the sections on glass slides. Following Hematoxylin-Eosin staining, the sections were seen at 40X magnification and captured on camera using a light microscope.

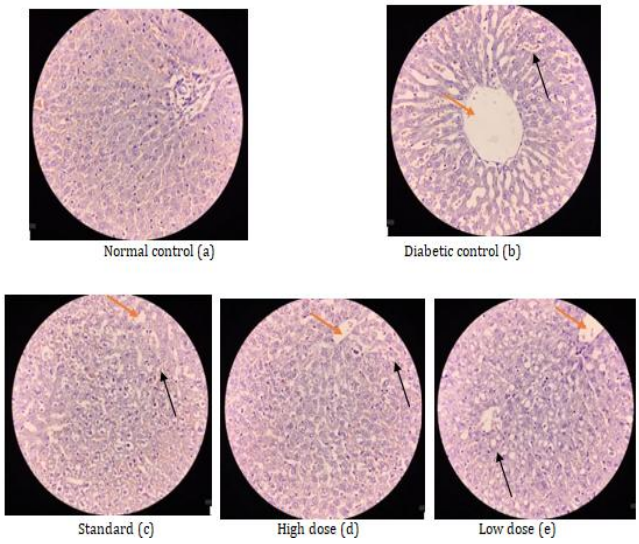

Figure 10: Histology of Liver

(a)Normal control rats had normal liver architecture whose hepatic lobules had a uniform pattern of polyhedral hepatocytes (b) Diabetic control rats showed disrupted arrangement and degeneration of hepatocytes and massive vacuolization (indicated by orange arrows) in the lobules and increased glycogen deposition (indicated by black arrows). (c-e) Glibenclamide- and SKF-treated rats showed a remarkable degree of preservation of the cellular arrangement with only mild vacuolization in the lobules and decreased glycogen deposition.

Histology of Pancreas

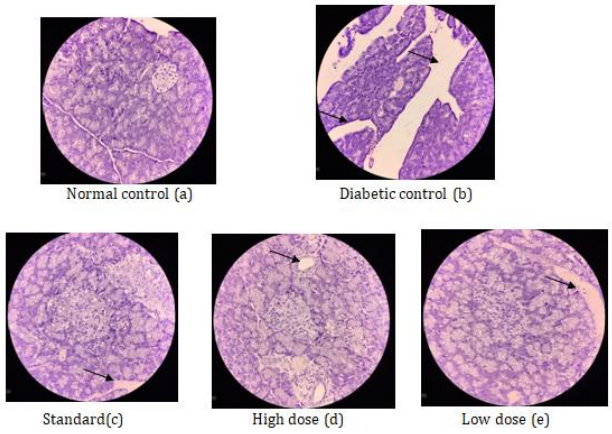

Figure 11: Histology of Pancreas

Fig 11(a) shows normal architecture of the pancreatic tissue and in fig 11 (b) pancreatic section of diabetic rat showing degenerative changes in the islets and β cells.

Fig 11(c) section of pancreatic tissue from a diabetic rat treated with glibenclamide and Fig 11(d) and 11(e) of test group showing restored to near normal architecture after the treatment period.

Antioxidant Tests Using Biomarkers

Estimation of SOD and CATALASE

The diabetic control group showed a marked reduction in **SOD and CAT activities** in the liver, kidney and pancreas compared with the normal control, indicating impaired antioxidant defence associated with diabetes. Treatment with Snehakanthi improved these antioxidant enzymes in all three tissues. At **400 mg/kg**, Snehakanthi significantly increased SOD activity in the **liver and pancreas (p<0.05)** and CAT activity in the **liver (p<0.01) and pancreas (p<0.001)** compared with the diabetic control. The 400 mg/kg dose also produced greater improvement than the 200 mg/kg dose in most parameters, suggesting that Snehakanthi, particularly at the higher dose, **attenuated diabetes-associated oxidative stress by enhancing endogenous antioxidant defence**. (as shown in table 05 and figures 12,13)

Table 05: Estimation of SOD and CATALASE

Groups	SOD (U/mg)			CAT (U/mg)		
	Liver	Kidney	Pancreas	Liver	Kidney	Pancreas
Group I – Normal control	8.68 ± 0.46	14.62 ± 0.76	4.86 ± 0.38	81.23 ± 3.86	36.74 ± 2.88	18.12 ± 0.92
Group II – Diabetic control	4.26 ± 0.38	9.86 ± 0.72	2.41 ± 0.16	43.26 ± 2.74	29.26 ± 3.18	7.78 ± 0.70
Group III – STZ + GBC (10 mg/kg)	8.04 ± 0.48*	13.84 ± 0.66*	4.18 ± 0.28*	74.84 ± 4.80***	31.98 ± 2.32	14.64 ± 0.68***
Group IV – STZ + SKF (200 mg/kg)	6.84 ± 0.42*	11.68 ± 0.68	3.80 ± 0.24*	67.36 ± 3.23**	30.76 ± 2.86	12.62 ± 0.60**
Group V – STZ + SKF (400 mg/kg)	7.86 ± 0.44*	13.58 ± 0.64	4.02 ± 0.30*	73.86 ± 4.52***	31.55 ± 2.28	14.20 ± 0.62***

Values are given as mean ± SEM (n=5).

*p<0.05, **p<0.01, ***p<0.001 when compared to diabetic control group (two-way ANOVA followed by Dunnett test)

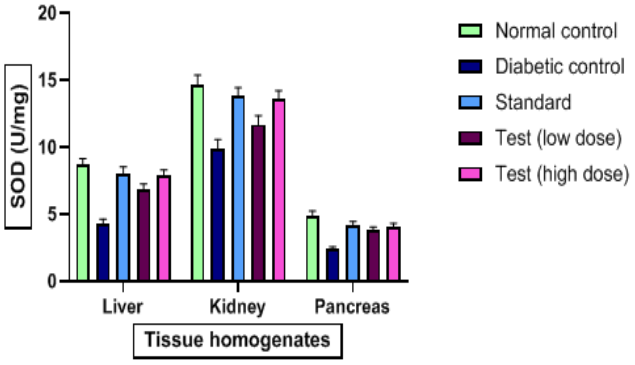

Figure 12: Estimation of SOD

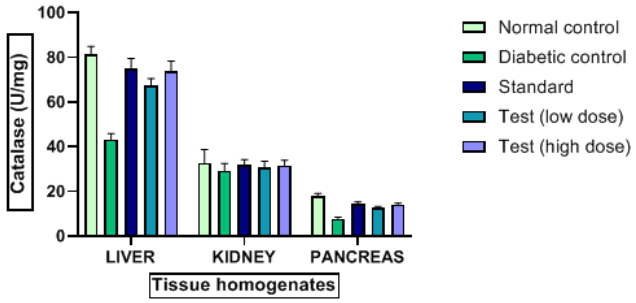

Figure 13: Estimation of CATALASE

Estimation of GSH and GPx

The diabetic control group showed a marked reduction in **GPx activity and GSH levels** in the liver, kidney and pancreas compared with the normal control, indicating impaired endogenous antioxidant defence. Treatment with Snehakanthi significantly improved both parameters. At **400 mg/kg**, Snehakanthi significantly increased GPx activity in the **liver (p<0.001), kidney (p<0.001) and pancreas (p<0.01)**, while GSH levels were significantly increased in the **liver (p<0.001), kidney (p<0.01) and pancreas (p<0.05)** compared with diabetic control. The higher dose generally produced greater improvement than 200 mg/kg, indicating that Snehakanthi, particularly at **400 mg/kg, enhanced tissue antioxidant defence and attenuated diabetes-associated oxidative stress**. (as shown in table 06 and figures 14,15)

Table 06: Estimation of GSH and GPx

Groups	GPx(U/mg protein)			GSH(µmol/g)		
	Liver	Kidney	Pancreas	Liver	Kidney	Pancreas
Group I Normal control	9.72± 0.48	7.70± 0.40	5.78± 0.36	2.86± 0.08	1.76± 0.04	3.48± 0.10
Group II diabetic control	4.46± 0.40	4.48± 0.22	3.48± 0.18	0.48± 0.02	0.24± 0.05	1.78± 0.44
Group III STZ+GBC (10mg/kg)	8.78± 0.38***	7.32± 0.42**	5.28± 0.32**	2.49± 0.20***	1.55± 0.18**	2.96± 0.14*
Group IV Group IV STZ + SKF (200mg/kg)	7.24± 0.34**	6.08± 0.35*	4.10± 0.26*	1.65± 0.08**	0.98± 0.12*	1.90± 0.36
Group V STZ+SKF(400mg/kg)	8.52± 0.40***	7.20± 0.32***	5.27± 0.32**	2.32± 0.06***	1.48± 0.06**	2.88± 0.24*

Values are given as mean ± SEM (n=5).

*p<0.05, **p<0.01, ***p<0.001 when compared to diabetic control group (two-way ANOVA followed by Dunnett test).

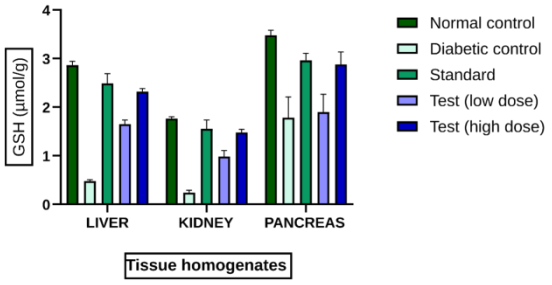

Figure 14: Estimation of GSH

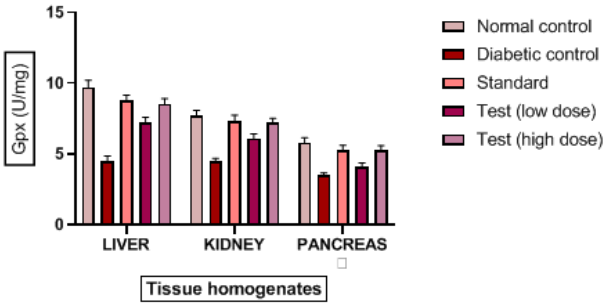

Figure 15: Estimation of GPx

DISCUSSION

The present study evaluated the antidiabetic and antioxidant effects of Snehakanthi, a proprietary polyherbal formulation containing *Salacia reticulata, Trigonella foenum-graecum, Tribulus terrestris, Strychnos potatorum* and *Phyllanthus emblica*, in streptozotocin (STZ)-induced diabetic rats. The formulation demonstrated beneficial effects across multiple parameters, including fasting blood glucose (FBG), oral glucose tolerance, body weight, tissue antioxidant status and hepatic and pancreatic histopathology.

The acute oral toxicity study showed that Snehakanthi was well tolerated up to 2000 mg/kg, with no mortality, apparent behavioural abnormalities or gross morphological changes in the examined organs during the observation period. Based on this safety assessment, 200 and 400 mg/kg doses were selected for the antidiabetic study.

STZ administration produced a marked diabetic state, with progressive elevation of FBG in the diabetic control group throughout the 28-day study. Snehakanthi treatment produced a progressive reduction in FBG, with the 400 mg/kg dose exhibiting a highly significant reduction (**p<0.0001**) in FBG on day 28 when compared with the diabetic control group. These findings demonstrate significant antihyperglycaemic activity of Snehakanthi, particularly at 400 mg/kg.

The findings of the OGTT further supported the antihyperglycaemic effect. Diabetic control animals exhibited marked elevation of blood glucose following glucose administration and a delayed decline during the 120-min observation period. In contrast, Snehakanthi at 400 mg/kg significantly reduced blood glucose (**p<0.0001)** at 60, 90 and 120 min compared with diabetic control, indicating improved glucose tolerance. The higher dose produced a response approaching that of glibenclamide, suggesting that Snehakanthi may improve glucose tolerance in addition to reducing fasting hyperglycaemia.

STZ-induced diabetes was also associated with progressive loss of body weight in the diabetic control group. Treatment with Snehakanthi attenuated this decline, with the 400 mg/kg group showing a significant increase (**p<0.0001**) in body weight compared with diabetic control on day 28. **The improvement in body weight together with the reduction in FBG and improvement in glucose tolerance indicates an overall improvement in the metabolic status of the treated animals**.

The histopathological findings were consistent with the biochemical results. Diabetic control animals showed disrupted hepatic architecture, hepatocellular degeneration and vacuolar changes, whereas Snehakanthi-treated animals showed comparatively preserved hepatic architecture and reduced apparent pathological alterations. Similarly, pancreatic sections from diabetic control animals showed degenerative changes in the islets and β-cell regions, while the Snehakanthi-treated groups showed comparatively preserved pancreatic architecture. These findings suggest that **the antihyperglycaemic effect of Snehakanthi was accompanied by attenuation of diabetes-associated hepatic and pancreatic tissue alterations.**

STZ-induced diabetes was associated with impairment of endogenous antioxidant defence, as evidenced by reduced SOD, CAT, GSH and GPx levels in the liver, kidney and pancreas of diabetic control animals. Treatment with Snehakanthi improved several of these antioxidant parameters. At 400 mg/kg, SOD activity was significantly increased in the liver and pancreas (**p<0.05**), while CAT activity showed significant improvement in the liver (**p<0.01**) and pancreas (**p<0.001**) compared with diabetic control. Similarly, Snehakanthi at 400 mg/kg significantly improved GPx activity in the liver (**p<0.001**), kidney (**p<0.001**) and pancreas (**p<0.01**) while GSH levels were also significantly increased in the liver (**p<0.001**), kidney (**p<0.01**) and pancreas (**p<0.05**) compared with diabetic control. These findings indicate that **Snehakanthi enhanced endogenous antioxidant defence in multiple tissues affected by diabetes.**

The antioxidant activity may be related to the phytochemical composition of the constituent plants. Phenolic and flavonoid compounds reported in the constituent plants may contribute to free-radical scavenging and enhancement of endogenous antioxidant defence. The observed improvement in antioxidant biomarkers, together with improved glycaemic control and histopathological findings, suggests that the antidiabetic activity of Snehakanthi may be associated with attenuation of diabetes-induced oxidative stress.

Overall, the findings demonstrate a consistent beneficial effect of Snehakanthi across glycaemic, metabolic, antioxidant and histopathological endpoints. The 400 mg/kg dose produced significant improvements in FBG, OGTT, body weight and multiple antioxidant biomarkers, with accompanying preservation of hepatic and pancreatic morphology. Although glibenclamide produced a stronger antihyperglycaemic response for these parameters, the results support the potential of Snehakanthi as a polyherbal intervention for experimental diabetes.

LIMITATIONS

This study did not measure serum insulin levels or directly evaluate pancreatic β-cell function. Key signalling pathways (e.g., PI3K/Akt, NFκB) and the specific contributions of individual phytochemicals (gallic acid, quercetin, ellagic acid, and epicatechin) remain uncharacterized.

FUTURE SCOPE

- Conduct qRT-PCR and Western blot analysis to quantify antioxidant-related gene and protein expression (SOD1, CAT, GPX1, NFκB, PI3K/Akt).
- Perform bioassay-guided fractionation to isolate and test individual active constituents of Snehakanthi.
- Further evaluation in suitable insulin resistance and type 2 diabetes models should precede appropriately designed human clinical studies.

CONCLUSION

The present study demonstrates that Snehakanthi, a proprietary polyherbal formulation containing *Salacia reticulata, Trigonella foenum-graecum, Tribulus terrestris, Strychnos potatorum* and *Phyllanthus emblica*, exhibits promising antidiabetic and antioxidant activity in streptozotocin-induced diabetic rats. Oral administration of Snehakanthi, particularly at 400 mg/kg, significantly reduced fasting blood glucose, improved oral glucose tolerance and attenuated diabetes-associated body-weight loss. These biochemical improvements were accompanied by enhancement of endogenous antioxidant defence, as reflected by improvements in SOD, CAT, GSH and GPx, together with comparatively preserved hepatic and pancreatic histoarchitecture.

The findings suggest that the beneficial effects of Snehakanthi may involve a combination of antihyperglycaemic and antioxidant actions arising from the bioactive constituents of its component plants. Overall, the results provide preliminary experimental evidence supporting the therapeutic potential of Snehakanthi in diabetes and warrant further investigation involving phytochemical standardization, mechanistic studies, quantitative histopathological assessment and longer-term evaluation of its efficacy and safety.

ACKNOWLEDGEMENT

1. **Navajyothi Sree Karunakara Guru Research Centre for Ayurveda and Siddha (NSKGRCAS)**: Provided the Ayurvedic product **Snehakanthi formulation**, along with financial support to share the research expenses.
2. **Santhigiri Ayurveda and Siddha Vaidyasala** : Licensed manufacturer.
3. **Nirmala College of Pharmacy**: Conducted the experimental design, animal studies, and data analysis.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

INFORMED CONSENT

Not applicable, as the study did not involve human participants

ETHICAL STATEMENT

All experimental procedures involving animals were carried out according to standard laboratory ethical guidelines and institutional regulations

AUTHOR CONTRIBUTION

Badmanaban R contributed to the conceptualization, supervision, and provided research guidance, Elayath Parvathy Murali participated in the experimental work, data collection, data analysis, literature review and manuscript preparation of the study, Brahmadathan U was involved in the review and editing of the manuscript.

REFERENCES

1. Mohd S, Kumar LL, Harish V, Kumar R, Chaudhary A, Sharma V. Diabetes mellitus: Complications, emerging therapeutic targets, and evolving treatment approaches. Obes Med. 2025;58:100652.
2. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119.
3. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33(1):S62-S69.
4. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2023. Diabetes Care. 2023;46(1):S19-S40
5. International Diabetes Federation. IDF Diabetes Atlas. 7th ed. Brussels: International Diabetes Federation; 2015.
6. Kharroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. World J Diabetes. 2015;6(6):850-867.
7. Tripathi UN, Verma J. Plants as anti-diabetic agents: A review. Asian J Pharm Clin Res. 2014;7(1):1-8.
8. Peiris DSHS, Fernando DTK, Senadeera SPNN, Ranaweera CB. A comprehensive review of *Salacia reticulata*: botanical, ethnomedicinal, phytochemical, and pharmacological insights. Asian Plant Res J. 2023;11(6):27-43.
9. Parveen R, Shamsi TN, Singh G. *Phyllanthus emblica* : a comprehensive review of its phytochemical composition and pharmacological properties. Front Pharmacol. 2023;14:1288618.
10. Hossen SM, Sarkar RM, Mahmud S, Aziz NMA. Medicinal potential of *Phyllanthus emblica* (Linn.) fruits extracts: biological and pharmacological activities. J Pharm Res Int. 2014;4(12):1486-1499.
11. Kuo MY, Ou HC, Lee WJ, Kuo WW, Hwang LL, Song TY. Ellagic acid inhibits oxidized low-density lipoprotein (OxLDL)-induced metalloproteinase (MMP) expression by modulating the protein kinase C-α/extracellular signal-regulated kinase/peroxisome proliferator-activated receptor γ/nuclear factor-κB (PKC-α/ERK/PPAR-γ/NF-κB) signaling pathway in endothelial cells. J Agric Food Chem. 2011;59(9):5100-5108.
12. Ramírez-Sánchez I, Maya L, Ceballos G, Villarreal F. (-)-Epicatechin prevents TNFα-induced activation of signaling cascades involved in inflammation and insulin sensitivity in 3T3-L1 adipocytes. J Nutr Biochem. 2012;23(7):800-807.
13. Kahkeshani N, Farzaei F, Fotouhi M, Alavi SS, Bahramsoltani R, Naseri R. Pharmacological effects of gallic acid in health and diseases: A mechanistic review. Iran J Basic Med Sci. 2019;22(3):225-237.
14. Organisation for Economic Co-operation and Development. Test No. 423: Acute oral toxicity—acute toxic class method. OECD Guidelines for the Testing of Chemicals, Section 4. Paris: OECD Publishing; 2002.
15. El-Bahr SM. Curcumin regulates gene expression of insulin like growth factor, B-cell CLL/lymphoma 2 and antioxidant enzymes in streptozotocin induced diabetic rats. BMC Complement Altern Med. 2013;13:368.
16. Assefa F, Seifu D, Makonnen E. Antihyperglycemic and antihyperlipidemic activities of ethanol extract of *Ajuga remota* Benth (Harmegusa) leaves in streptozotocin induced diabetic rats. Afr J Pharm Pharmacol. 2017;11(2):17-24.
17. Muthukrishnan S, Sivakkumar T, Anbiah V. Biological evaluation, isolation, and characterization of novel polyphenol derivatives from *Schleichera oleosa* (Lour) Oken as anti-diabetic agents. Curr Bioact Compd. 2022;18(2):1-14.
18. Kim MJ, Ha BJ. Antihyperglycemic and antihyperlipidemic effects of fermented *Rhynchosia nulubilis* in alloxan-induced diabetic rats. Toxicol Res. 2013;29(1):15-19.
19. Ali AH, et al. Assessment of Toxicity and Therapeutic Effects of Goose Bone in a Rat Model. J Chem. 2019;2019:1943601.
20. Misra HP and Fridovich I. Superoxidedismutase : positive spectrophotometric assays. Anal. Biochem. 1977;79:553–560
21. Ogata M, Takahara S. Paper Electrophoretic Studies on the Catalase Protein in Acatalasemic Blood Extract (Stage 3 by Herbert-Pinsent). Proceedings of the Japan Academy. 1962;38(7):361–4.
22. Moron MS, Depierre JW, Mannervik B. Levels of glutathione, glutathione reductase and glutathione S-transferase activities in rat lung and liver. Biochim. Biophys. Acta. 1979;582(1):67–78.
23. Wendel A. Glutathione Peroxidases in enzymatic basis of detoxification. Academic Press, New York. 1980;333–353.