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Evaluation of Anti-diabetic activity of *Salacia oblonga* in Streptozotocin Induced diabetic model in Wistar Rats

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ABSTRACT:
Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and associated disturbances in carbohydrate and lipid metabolism, necessitating the development of effective and safe therapeutic agents. The present study evaluated the antioxidant and antidiabetic potential of *Salacia oblonga* extracts using in vitro and streptozotocin-induced diabetic Wistar rat models. Root, stem, and leaf extracts were prepared using 80% aqueous methanol and subjected to phytochemical screening, antioxidant assays, and α-glucosidase and α-amylase inhibition studies. Among the evaluated extracts, the root extract from Eleshwaram (SREE) demonstrated the highest phenolic and flavonoid contents and superior antioxidant activity, including DPPH radical scavenging and ferric reducing capacity. The extract also exhibited significant inhibition of carbohydrate-hydrolyzing enzymes, indicating its potential to reduce postprandial hyperglycemia. In streptozotocin-induced diabetic rats, oral administration of *S. oblonga* root extract produced a dose-dependent reduction in random and postprandial blood glucose levels, with the 400 mg/kg dose showing an antihyperglycemic effect comparable to metformin. Treatment additionally improved lipid parameters and serum creatinine and bilirubin levels, suggesting beneficial effects against diabetes-associated metabolic and organ dysfunction. Histopathological examination revealed progressive restoration of pancreatic islet architecture and β-cell regeneration, particularly at 400 mg/kg. The extract was also reported to be safe up to 2000 mg/kg in acute toxicity evaluation. Overall, the findings demonstrate that *Salacia oblonga*, particularly its root extract, possesses promising multitarget antidiabetic and antioxidant properties and may serve as a potential natural source for the development of phytotherapeutic agents for the management of type 2 diabetes mellitus.

1. INTRODUCTION:
Blood glucose homeostasis is maintained through the coordinated actions of insulin and glucagon, the two principal hormones regulating glucose metabolism. Insulin, secreted by pancreatic β-cells in response to elevated

blood glucose levels, promotes cellular glucose uptake through glucose transporters, thereby reducing circulating glucose concentrations. Conversely, glucagon, secreted by pancreatic α-cells during hypoglycemia, stimulates hepatic glucose production to maintain normal blood glucose levels. Disruption of insulin secretion or impaired insulin action results in diabetes mellitus, a chronic metabolic disorder characterized by persistent hyperglycemia and abnormalities in carbohydrate, lipid, and protein metabolism. [2,3]

Diabetes mellitus is one of the fastest-growing global health challenges, with its prevalence increasing rapidly worldwide. The International Diabetes Federation estimated that 382 million individuals were affected by diabetes in 2013, with projections reaching 592 million by 2035. India alone accounts for approximately 62 million diabetic patients, making it one of the countries with the highest disease burden [3,5]. Diabetes is broadly classified into Type I diabetes mellitus (T1DM), caused by autoimmune destruction of pancreatic β-cells leading to absolute insulin deficiency, and Type II diabetes mellitus (T2DM), characterized by insulin resistance and impaired insulin secretion [3]. T2DM represents nearly 90–95% of all diabetes cases and is frequently associated with obesity, sedentary lifestyle, and genetic predisposition [3,5].

Persistent hyperglycemia contributes to several metabolic disturbances, including oxidative stress, dyslipidemia, increased hepatic glucose production, impaired glucose uptake by peripheral tissues, enhanced intestinal glucose absorption, and increased renal glucose reabsorption. These abnormalities ultimately result in chronic complications such as cardiovascular diseases, nephropathy, retinopathy, neuropathy, and diabetic ketoacidosis. Therefore, effective glycemic control remains the primary objective in diabetes management [6-9].

Several classes of synthetic hypoglycemic agents, including sulfonylureas, biguanides, α-glucosidase inhibitors, thiazolidinediones, and sodium-glucose co-transporter-2 (SGLT-2) inhibitors, are widely employed to manage hyperglycemia through different mechanisms such as enhancing insulin secretion, improving insulin sensitivity, delaying carbohydrate digestion, or reducing renal glucose reabsorption. Although these drugs effectively lower blood glucose levels, their long-term use is often associated with adverse effects such as hypoglycemia, gastrointestinal disturbances, weight gain, hepatotoxicity, cardiovascular complications, and secondary therapeutic failure, limiting their clinical utility [6-9].

Medicinal plants have gained considerable attention as alternative therapeutic agents because of their broad pharmacological activities, affordability, and comparatively lower incidence of adverse effects. The World Health Organization has also recognized the importance of medicinal plants in the management of diabetes, particularly in developing countries . More than 1,200 plant species have been traditionally used for diabetes management, of which nearly 400 have undergone scientific evaluation. Plant-derived bioactive compounds exert antidiabetic effects through multiple mechanisms, including stimulation of pancreatic β-cells, enhancement of insulin sensitivity, inhibition of α-glucosidase activity, suppression of gluconeogenesis, promotion of glycogen synthesis, and reduction of oxidative stress [10-12]. Owing to their multitarget therapeutic potential and improved safety profile, medicinal plants continue to serve as an important source for the discovery and development of novel antidiabetic agents.

Salacia oblonga is a vulnerable medicinal plant belonging to the family Celastraceae, distributed mainly in India and Sri Lanka, and extensively used in Ayurvedic medicine for the management of diabetes and other metabolic disorders. The roots and stems contain several bioactive compounds, including salacinol, kotalanol, flavonoids, phenolics, tannins, triterpenoids, and sterols**,** which are primarily responsible for its potent α-glucosidase inhibitory activity and consequent reduction of postprandial hyperglycemia [12]**.** Experimental and clinical studies have demonstrated that *S. oblonga* exhibits significant antidiabetic, antioxidant, anti-inflammatory, antihyperlipidemic, cardioprotective, nephroprotective, antimicrobial, antimutagenic, and cytotoxic activities [13,14,15]**.** Furthermore, the plant has shown a favorable safety profile with no significant toxic or genotoxic effects in preclinical and clinical investigations [14]**,** making it a promising natural source for the development of novel antidiabetic therapeutics and the management of diabetes-associated complications.

2. MATERIALS AND METHODS:

2.1 Materials

2.1.1 Chemicals

Analytical-grade chemicals and reagents, including 1,1-diphenyl-2-picrylhydrazyl (DPPH), potassium hexaferrocyanate, trichloroacetic acid, ferric chloride, sodium acetate, 2,4,6-tripyridyl-s-triazine (TPTZ), sodium

nitroprusside, sulfanilamide, naphthylethylenediamine dihydrochloride, Folin–Ciocalteu reagent, sodium carbonate, gallic acid, quercetin, sodium nitrite, aluminium chloride, sodium hydroxide, thiobarbituric acid, phosphate salts, NADH, nitro blue tetrazolium, phenazine methosulfate, ammonium molybdate, ferrous chloride, ferrozine, 2-deoxy-D-ribose, potassium hydroxide, EDTA, hydrogen peroxide, butylated hydroxytoluene, xylenol orange, ammonium ferrous sulphate, and p-nitrophenyl-α-D-glucopyranoside were procured from HiMedia Laboratories Pvt. Ltd., Mumbai, India. Methanol, ethanol, dimethyl sulphoxide (DMSO), hydrochloric acid, and sulphuric acid were obtained from Merck, while acarbose and α-glucosidase enzyme (EC 3.2.1.20) were purchased from Sigma-Aldrich, USA.

2.1.2 Collection of Plant Material

Salacia oblonga plants were collected from Eleshwaram (Andhra Pradesh), Tuticorin (Tamil Nadu), and Karwar (Karnataka), India. The plant material was authenticated by Department of Dravyagunavigyan, P.D.E.A College of Ayurved and research Centre, Nigdi, Pune, maintained in the greenhouse, shade-dried, and stored for further studies.

2.1.3 Animal Ethical Clearance

All animal experiments were conducted following the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India, after approval from the Institutional Animal Ethics Committee (IAEC approval no. SCOP/IAEC/2025/12).

2.2 Methods

2.2.1 Preparation of Plant Extracts

Shade-dried roots, stems, and leaves of *S. oblonga* were powdered and extracted by hot reflux using 80% aqueous methanol (100 g plant material; three extraction cycles of 3 h each). The combined filtrates were concentrated under reduced pressure using a rotary evaporator and lyophilized to obtain dry extracts. The extracts were labeled according to plant part and geographical source, stored at −20°C, and reconstituted in DMSO to obtain a final concentration of 1 mg/mL [16].

Figure 1: Plant material before extraction and after extraction.

2.2.2 Phytochemical Screening of *Salacia oblonga* Root Extracts

The *S. oblonga* root extracts were qualitatively screened for the presence of major phytoconstituents using standard phytochemical methods. The extracts were evaluated for phenols, flavonoids, alkaloids, saponins, cardiac glycosides, tannins, steroids, and terpenoids based on characteristic color changes or precipitate formation after treatment with their respective reagents. The presence of each phytochemical class was confirmed according to established qualitative screening protocols [16].

2.2.3 In Vitro Antioxidant and Antidiabetic Studies

The in vitro antioxidant and antidiabetic activities of *S. oblonga* root extracts collected from Eleshwaram (SREE), Tuticorin (SRET), and Karwar (SREK), along with stem (SSEE) and leaf (SLEE) extracts, were evaluated and compared using standard biochemical assays.

2.2.3.1 Estimation of Total Phenolic Content, Total Flavonoid Content, and Total Antioxidant Activity

Total phenolic content (TPC) was determined using the Folin–Ciocalteu method and expressed as gallic acid equivalents (GAE). Total flavonoid content (TFC) was estimated by the aluminium chloride colorimetric method using quercetin as the reference standard. Total antioxidant activity was assessed by the ferric reducing antioxidant power (FRAP) assay, based on the reduction of the Fe^{3+}–TPTZ complex to Fe^{2+}–TPTZ, and the results were expressed as tocopherol equivalents. Absorbance was recorded using a UV–Visible spectrophotometer following standard protocols [16].

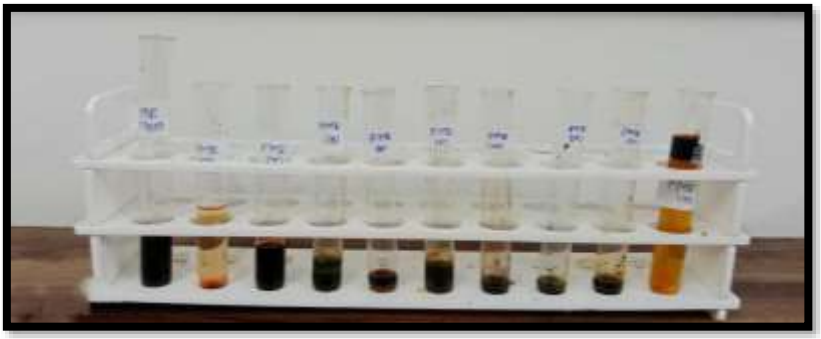


Figure 2: Phytochemical screening of *S. oblonga* root extracts (methanolic extract).

Figure 3: Phytochemical screening of *S. oblonga* stem extracts (methanolic extract).

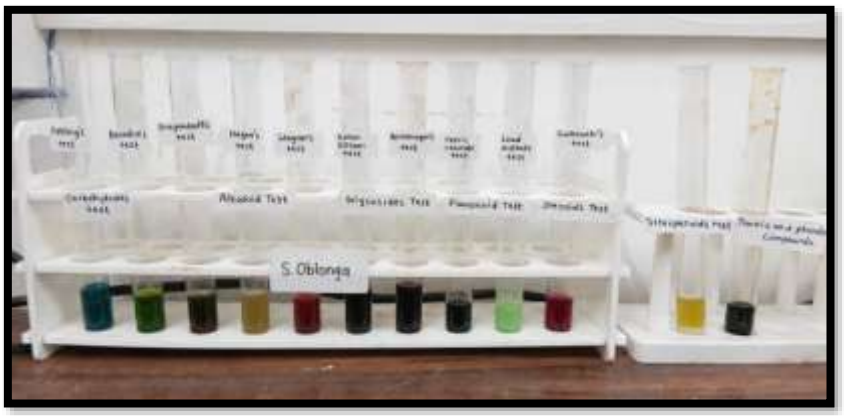


Figure 4: Phytochemical screening of *S. oblonga* leaf extracts (methanolic extract).

2.2.3.2 Scavenging Activities

The antioxidant potential of *S. oblonga* extracts was evaluated using standard free radical scavenging assays, including DPPH, nitric oxide (NO), superoxide, hydroxyl, and hydrogen peroxide scavenging methods. Different concentrations of the extracts (0–250 µg/mL) were tested, and absorbance was measured using a UV–Visible spectrophotometer at the respective wavelengths. Quercetin, curcumin, mannitol, and sodium pyruvate were used as reference standards where appropriate. Radical scavenging activity was expressed as percentage inhibition, and the IC_{50} values were determined from concentration–response curves by linear regression.

I. DPPH Free Radical Scavenging Assay

DPPH radical scavenging activity was determined by measuring the reduction of the stable DPPH radical at 517 nm after incubation with different concentrations of *S. oblonga* extracts. Quercetin served as the reference antioxidant [17].

II. Nitric Oxide Radical Scavenging Assay

Nitric oxide scavenging activity was assessed using the sodium nitroprusside–Griess reaction, and the chromophore formed was measured at 546 nm. Curcumin was used as the reference standard [18].

III. Superoxide Radical Scavenging Assay

Superoxide radical scavenging activity was evaluated using the PMS–NADH–NBT system, where inhibition of formazan formation was measured at 562 nm. Quercetin was used as the standard [19].

IV. Hydroxyl Radical Scavenging Assay

Hydroxyl radical scavenging activity was estimated using the deoxyribose degradation assay, and the resulting chromogen was measured at 532 nm. Mannitol served as the positive control [20].

V. Hydrogen Peroxide Scavenging Assay

Hydrogen peroxide scavenging activity was determined using the FOX reagent method, with absorbance recorded at 560 nm. Sodium pyruvate was used as the reference compound [21].

VI. Reducing Power, Thiobarbituric Acid, and Phosphomolybdenum Assays

The antioxidant potential of *S. oblonga* extracts was further evaluated using reducing power, thiobarbituric acid (TBA), and phosphomolybdenum assays following standard protocols. Reducing power was determined by measuring the reduction of ferric ions at 700 nm using curcumin as the reference standard. Lipid peroxidation inhibitory activity was assessed by the TBA assay, with absorbance recorded at 552 nm using ascorbic acid as the standard. Total antioxidant capacity was estimated by the phosphomolybdenum assay based on the reduction of Mo(VI) to Mo(V), and absorbance was measured at 695 nm using ascorbic acid as the reference compound [22,23].

VIII. Carbohydrate-Hydrolyzing Enzyme Inhibition Assays

The antidiabetic potential of *S. oblonga* extracts was evaluated by assessing the inhibition of α-glucosidase and α-amylase enzymes using standard in vitro methods. α-Glucosidase inhibition was determined using *p*-nitrophenyl-α-D-glucopyranoside as the substrate, while α-amylase inhibition was measured using the starch–dinitrosalicylic acid method. Absorbance was recorded at 405 and 540 nm, respectively, and acarbose was used as the reference standard. Enzyme inhibitory activity was expressed as percentage inhibition, and IC_{50} values were calculated from concentration–response curves using linear regression. [24,25]

For all antioxidant assays, the percentage radical scavenging activity was calculated using the following equation:

Percentage inhibition (%) = $[(A_0 - A_1)/A_0] \times 100$

where A_0 is the absorbance of the control and A_1 is the absorbance of the test sample. IC_{50} values were calculated from the corresponding inhibition curves.

2.2.4 Maintenance of Animals

Healthy male Albino Wistar rats (180–220 g, 10 weeks old) were procured from registered animal facility and housed under standard laboratory conditions (25–30°C, 45–55% relative humidity, and a 12 h light/dark cycle). Animals were acclimatized for one week before experimentation and maintained in polypropylene cages with free

access to standard pellet diet and water.

2.2.5 Dosage Preparation
Salacia oblonga root extract (SOE) was freshly suspended in 0.05% Tween-80 (150 mg/mL) and administered orally according to individual body weight. The extract and the standard drug, metformin, were administered twice daily for 14 days using an intragastric tube.

2.2.6 In Vivo Studies
2.2.6.1 Experimental Design
The doses of *Salacia oblonga* extract (200, 300, and 400 mg/kg) used in the present study were selected based on previously published pharmacological studies.[4-12]
A total of 36 Albino Wistar rats (30 diabetic and 6 normal) were randomly divided into six groups (n = 6): Group I, normal control; Group II, diabetic control; Group III, Metformin-treated (2 mg/kg); and Groups IV–VI, diabetic rats treated with *Salacia oblonga* extract (SOE) at doses of 200, 300, and 400 mg/kg body weight, respectively.

2.2.6.2 Induction of Type II Diabetes
Type II diabetes was induced in overnight-fasted Albino Wistar rats by intraperitoneal administration of streptozotocin (45 mg/kg body weight). Animals received 10% dextrose solution after STZ administration to prevent hypoglycemic shock. After 72 h, fasting blood glucose levels were measured, and rats with glucose levels ≥300 mg/dL were considered diabetic. A stabilization period of one week was allowed before initiating treatment [26].

2.2.6.3 Blood Sample Collection
Blood samples were collected from the retro-orbital plexus on days 0, 7, and 14 into EDTA-coated tubes. Samples were centrifuged at 3000 rpm for 15 min to separate plasma and serum, which were immediately used for biochemical analysis [27].

2.2.6.4 Biochemical Estimations
At predetermined intervals, plasma and serum biochemical parameters were estimated using commercially available diagnostic kits according to the manufacturers' instructions. Plasma glucose was determined by the glucose oxidase–peroxidase (GOD–POD) method at 505 nm. Serum total cholesterol and HDL-cholesterol were estimated enzymatically at 500 nm, while triglycerides were determined using the glycerol phosphate oxidase–peroxidase (GPO–POD) method at 546 nm. Serum creatinine was measured by the alkaline picrate (Jaffe) method at 520 nm, and total bilirubin was estimated by the diazo reaction at 540 nm. The concentrations of all biochemical parameters were calculated using the respective standard calibration formulas provided with the assay kits [28-31].

2.2.6.5 Histopathological Analysis
At the end of the experimental period, rats were euthanized under anesthesia, and pancreatic tissues were excised, fixed in 10% neutral buffered formalin, processed by routine paraffin embedding, sectioned (4–5 μm), and stained with hematoxylin and eosin (H&E). Histopathological changes, including degeneration of islets of Langerhans, β-cell depletion, necrosis, inflammatory cell infiltration, and tissue regeneration, were examined under a light microscope, and representative photomicrographs were recorded [32].

2.2.6.6 Statistical Analysis
All experimental data were expressed as mean ± SD (n = 6). Statistical analysis was performed using SigmaPlot version 11.0. Differences among groups were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's post hoc test, and values of $p < 0.05$ were considered statistically significant.

3. RESULTS:
3.1 Phytochemical Analysis of *Salacia oblonga* Root Extracts
Qualitative phytochemical screening revealed the presence of phenols, flavonoids, alkaloids, saponins, steroids, and terpenoids in all *S. oblonga* root extracts, whereas glycosides were absent. The Eleshwaram (SREE) and Tuticorin (SRET) extracts exhibited comparatively higher levels of phenols and saponins. SREE contained a higher concentration of alkaloids, while SRET showed relatively higher levels of steroids and terpenoids. In contrast, the Karwar extract (SREK) demonstrated comparatively lower levels of all detected phytoconstituents,

indicating regional variation in phytochemical composition.

3.2 Total Phenolic Content, Total Flavonoid Content, and Total Antioxidant Activity

The total phenolic content (TPC), total flavonoid content (TFC), and ferric reducing antioxidant power (FRAP) of S. oblonga root extracts varied among the three geographical regions. SREE exhibited the highest TPC (78.9 ± 2.1 µg GAE/250 µg extract) and TFC (83.2 ± 3.5 µg QE/250 µg extract), followed by SRET and SREK. Similarly, FRAP analysis demonstrated the greatest antioxidant activity in SREE (623.8 ± 4.3 µg tocopherol equivalents), which was comparable to SRET (620.9 ± 3.2 µg) and markedly higher than SREK (447.3 ± 3.8 µg). Overall, the antioxidant potential of the extracts followed the order SREE > SRET > SREK, indicating that geographical variation significantly influenced the phytochemical composition and antioxidant capacity of S. oblonga root extracts.

3.3 Scavenging Activities of *Salacia oblonga* Root Extracts

3.3.1 DPPH Radical Scavenging Assay

All *S. oblonga* root extracts exhibited concentration-dependent DPPH radical scavenging activity (50–250 µg/mL). At higher concentrations (150–250 µg/mL), SREE showed the strongest activity, followed by SRET and SREK. The maximum inhibition at 250 µg/mL was 82.8%, 64.0%, and 57.9% for SREE, SRET, and SREK, respectively. SREE also demonstrated the lowest IC_{50} value (140.0 ± 2.1 µg/mL), which was comparable to quercetin (133.3 ± 2.1 µg/mL), indicating superior antioxidant potential among the extracts.

3.3.2 Nitric Oxide Radical Scavenging Assay

Nitric oxide scavenging activity increased with increasing extract concentration in all samples. SREE exhibited the highest activity at 250 µg/mL (58.6%), followed by SRET (52.9%) and SREK (50.6%). The corresponding IC_{50} values were 183.0 ± 1.6, 190.6 ± 2.1, and 236.7 ± 2.3 µg/mL, respectively, while curcumin showed the greatest activity among the standards. Overall, SREE demonstrated the most potent nitric oxide scavenging activity, followed by SRET and SREK.

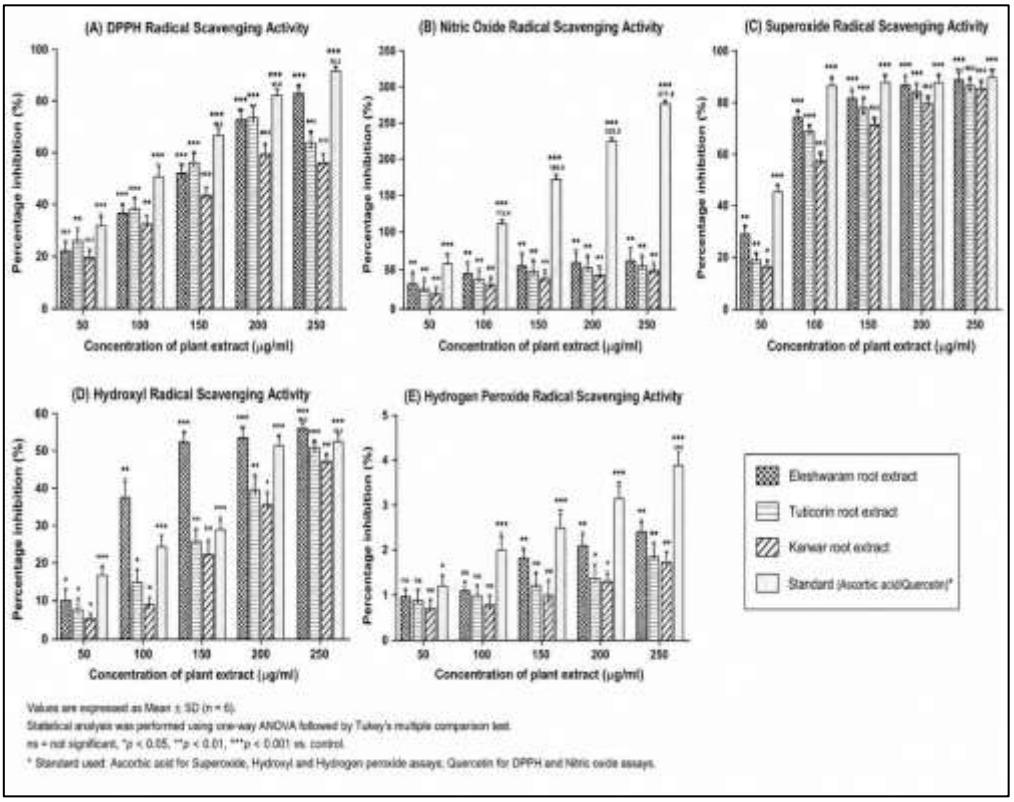


Figure 5: Percentage inhibition of various free radical scavenging activities by *S. oblonga* root extracts from three different regions: (A) DPPH, (B) Nitric oxide, (C) Superoxide, (D) Hydroxyl, and (E) Hydrogen peroxide radical scavenging assays. Values are expressed as mean ± SD (n = 6); *p*<0.05, **p*<0.01, ***p*<0.001 versus control.

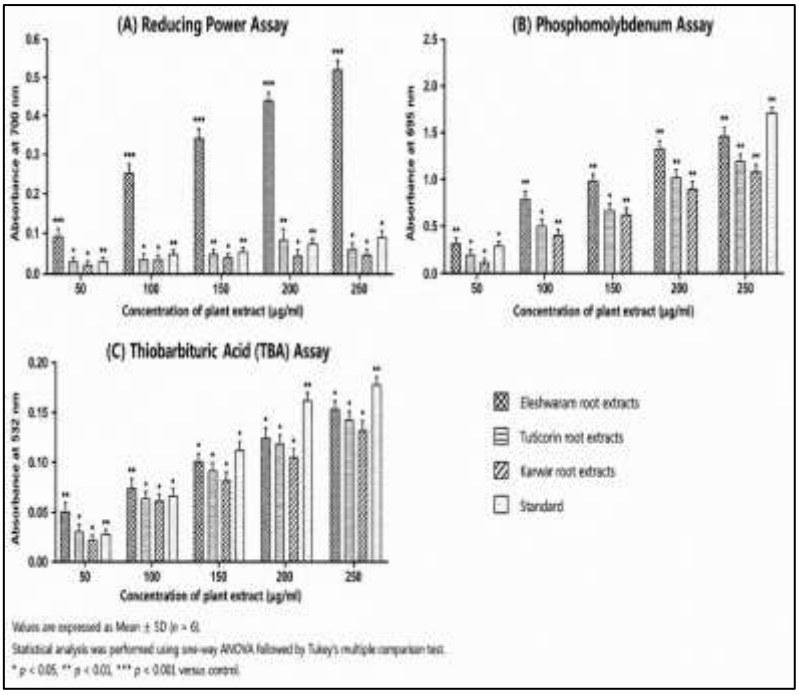


Figure 6: Graphs Showing Absorbance of Reducing Power, Phosphomolybdenum and

3.3.4 Thiobarbituric Acid Assays of *S. oblonga* Extracts of Three Different Regions

(A) Reducing power assay; (B) Phosphomolybdenum assay; (C) Thiobarbituric acid assay, standard used (reducing power assay – butylated hydroxytoluene, phosphor- molybdenum assay and thiobarbituric acid assay – ascorbic acid Values are expressed in mean ± SD (n=6) *p<0.05 vs Control; **p<0.01 vs Control; ***p<0.001 vs Control.

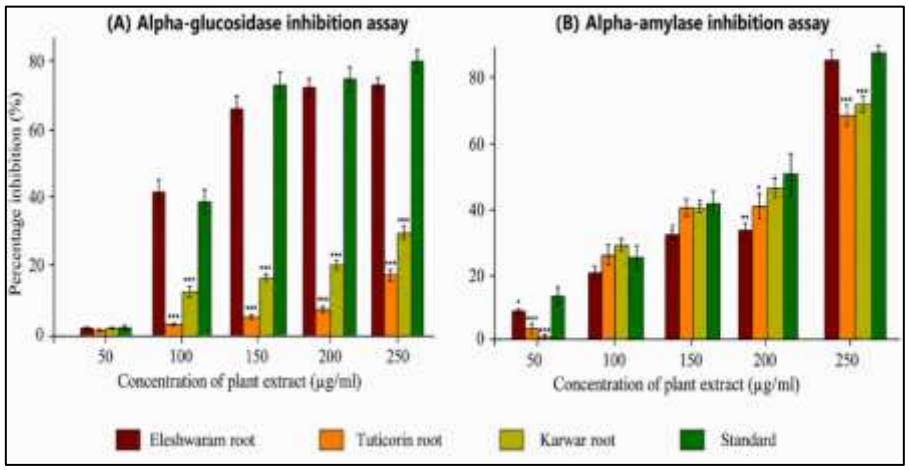


Figure 7: Carbohydrate-Hydrolyzing Enzymes Inhibition Activities of Root Extracts of *S. oblonga* of Three Different Regions

(A) Alpha-glucosidase inhibition assay; (B) Alpha-amylase inhibition assay Values are expressed in mean ± SD (n=6) *p<0.05 Vs Control; **p<0.01 Vs Control; ***p<0.001 Vs Control

3.3.5 Phytochemical Analysis of Root, Stem, and Leaf Extracts of *Salacia oblonga*

Phytochemical screening showed the presence of phenols, flavonoids, saponins, steroids, and terpenoids in all extracts, while alkaloids were detected only in the root and glycosides were absent. Overall, the root extract (SREE) exhibited the richest phytochemical profile, followed by the stem (SSEE) and leaf (SLEE) extracts.

Total Phenolic, Flavonoid, and Antioxidant Activity

The root extract (SREE) showed the highest total phenolic content (78.9 ± 2.1 µg GAE/250 µg), total flavonoid

content (83.2 ± 3.5 µg QE/250 µg), and FRAP antioxidant activity (623.8 ± 4.3 µg tocopherol equivalents), indicating superior antioxidant potential compared with the stem and leaf extracts

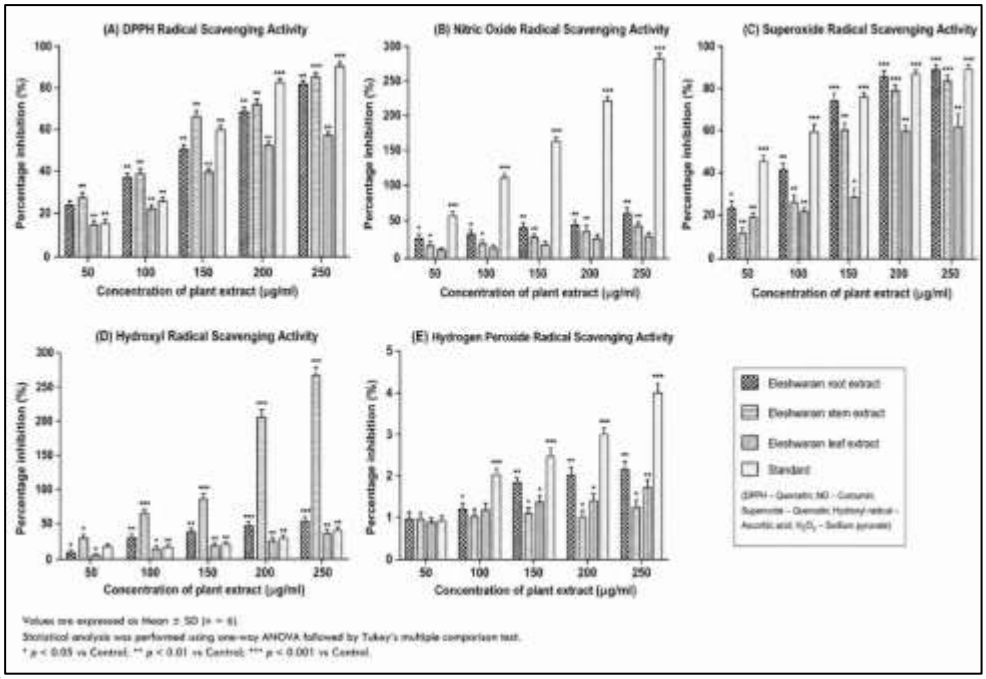


Figure 8: Percentage Inhibition of Free Radical Scavenging Activities of Root, Stem and Leaf Extracts of *S. oblonga*

(A) DPPH radical scavenging, (B) Nitric oxide radical scavenging, (C) Super oxide radical scavenging, (D) Hydroxyl radical scavenging, (E) Hydrogen peroxide radical SD – standard (DPPH – quercetin, NO – curcumin, SOD – quercetin, Hydroxyl radical – ascorbic acid, H_2O_2 – sodium pyruvate).
Values are expressed in mean ± SD (n=6); *p<0.05 vs Control; **p<0.01 vs Control;
***p<0.001 vs Control

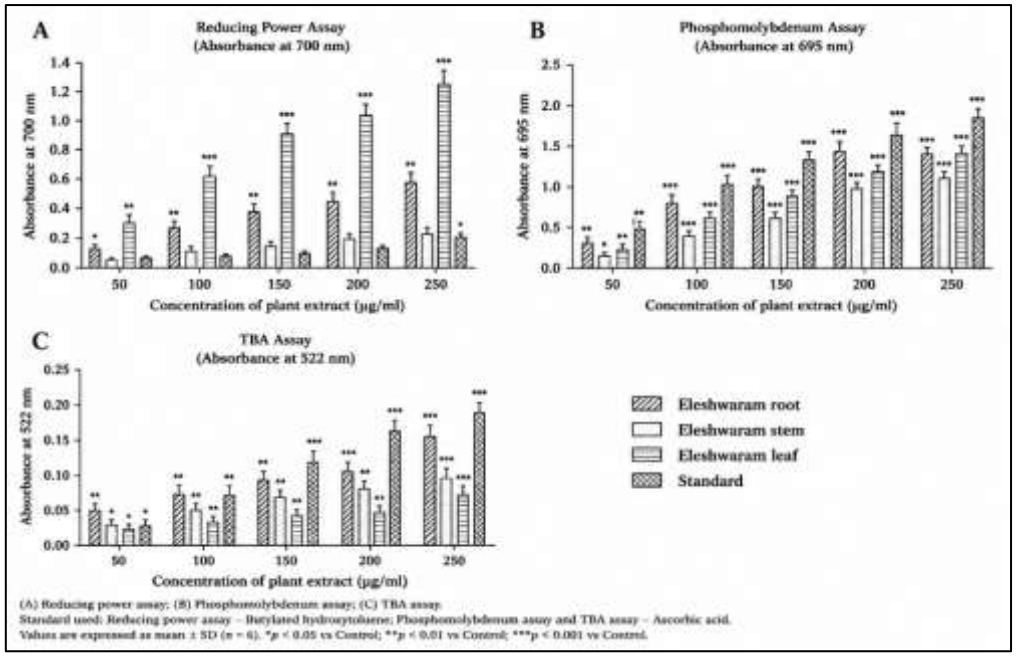


Figure 9: Graphs Showing Absorbance of Reducing Power, Phospho- molybdenum and TBA Assays of Root, Stem and Leaf Extracts of *S. oblonga*

(A) Reducing power assay; (B) Phosphomolybdenum assay; (C) TBA assay, standard used (reducing power assay – butylated hydroxytoluene, phosphor-molybdenum assay and TBA – ascorbic acid, Values are expressed in mean ± SD (n=6), *p<0.05 Vs Control; **p<0.01 Vs Control; ***p<0.001 Vs Control.
(B)

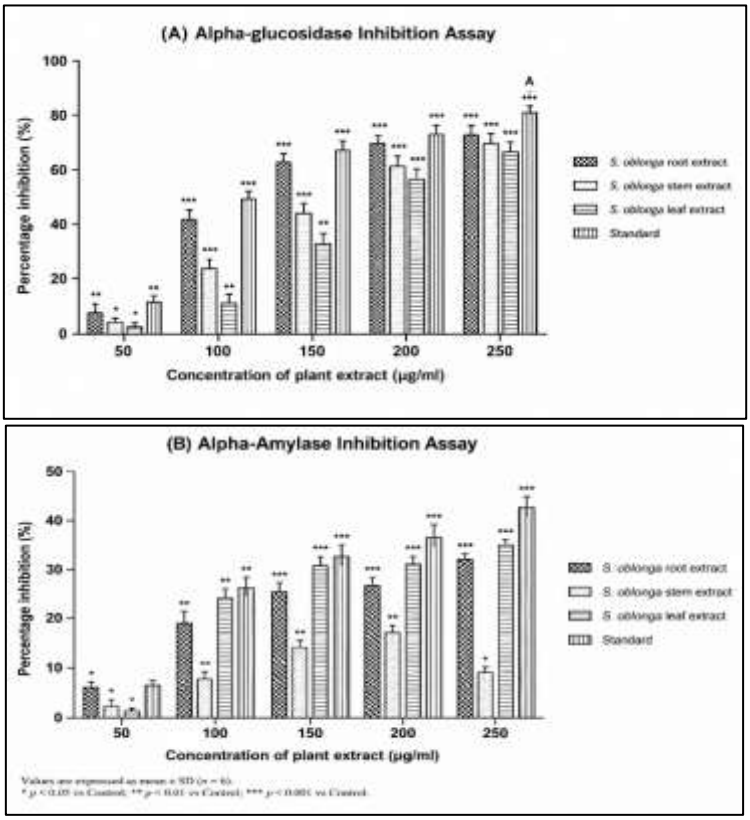
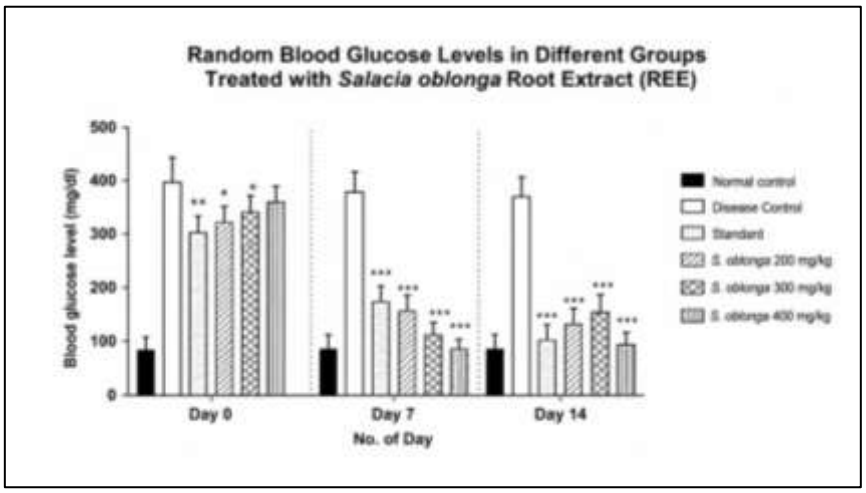


Figure 10: Carbohydrate-Hydrolyzing Enzymes Inhibition Activities of Root, Stem and Leaf Extracts of *S. oblonga*

3.4 In vivo Activity

3.4.1 Effect of *Salacia oblonga* Root Extract on Blood Glucose Levels

Treatment with *S. oblonga* root extract significantly reduced random and postprandial blood glucose levels in streptozotocin-induced diabetic rats compared with the diabetic control group. The antihyperglycemic effect was dose-dependent, with the 400 mg/kg dose producing the greatest reduction, comparable to the standard drug metformin by day 14, indicating effective improvement in glycemic control.



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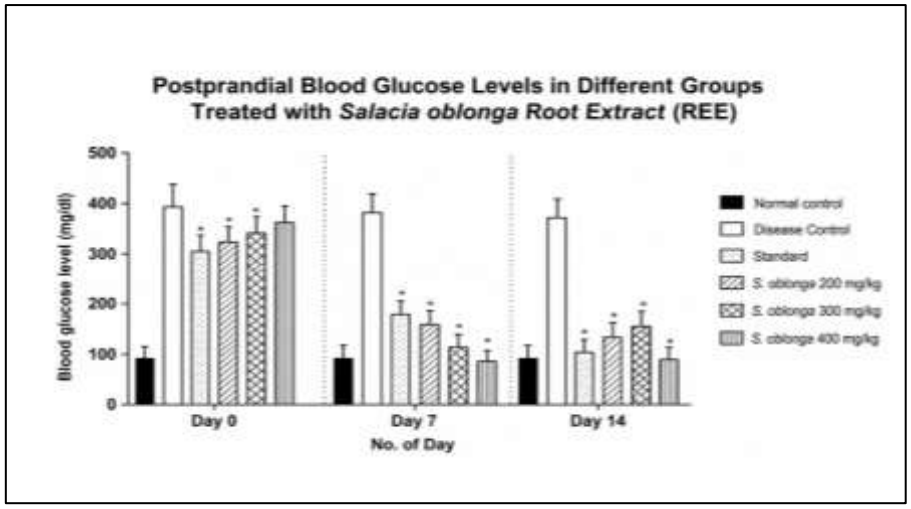
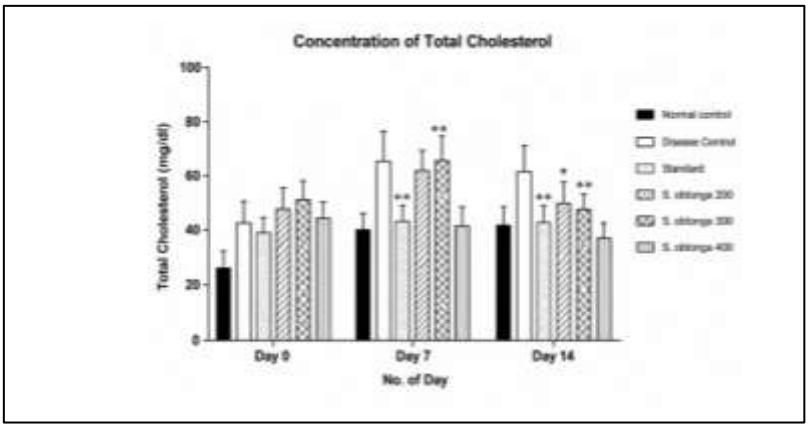
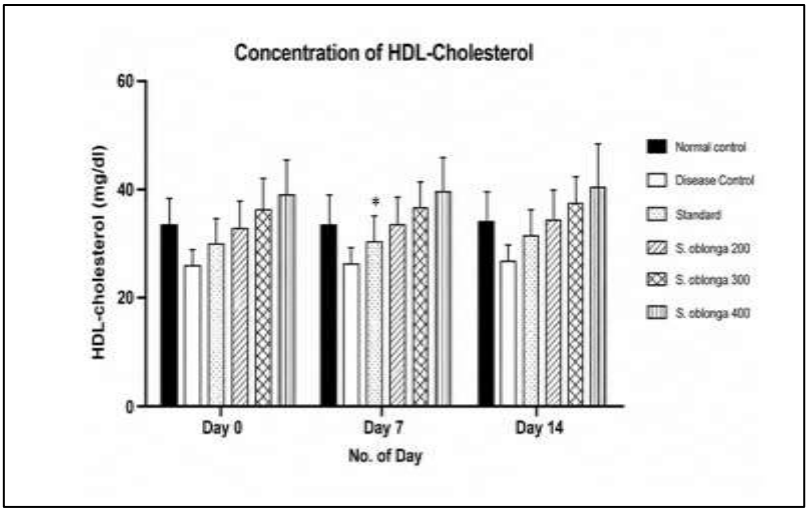


Figure 11: Graph Showing Concentration of Random and Postprandial Blood Glucose (mg/dl) in Different Groups Treated with SOE

3.4.2 Effect of *S. oblonga* Root Extracts on total Cholesterol, HDL-cholesterol and triglycerides in Experimental Rats





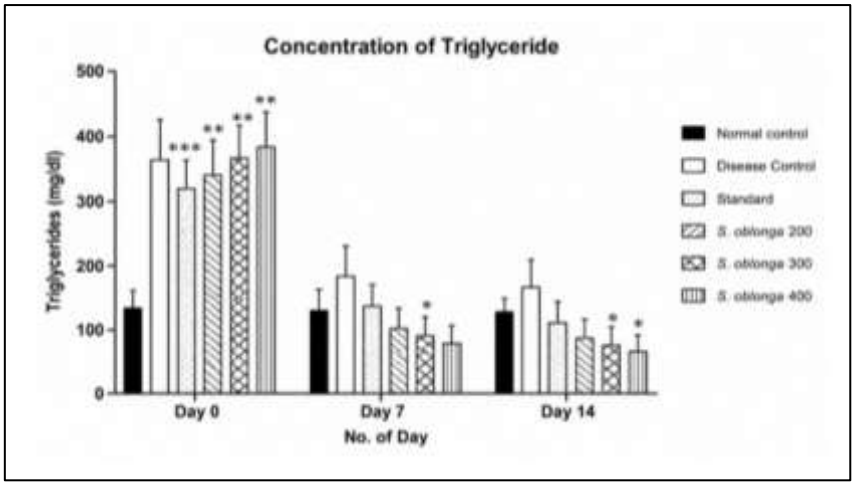


Figure 12: Graphs Showing Concentration of Total Cholesterol, HDL-Cholesterol, and Triglycerides (mg/dl) in Different Animal Groups Treated with Root Extracts of SOE

3.4.3 Effect of *S. oblonga* Root Extracts on Serum Creatinine and Total Bilirubin in Experimental Rats

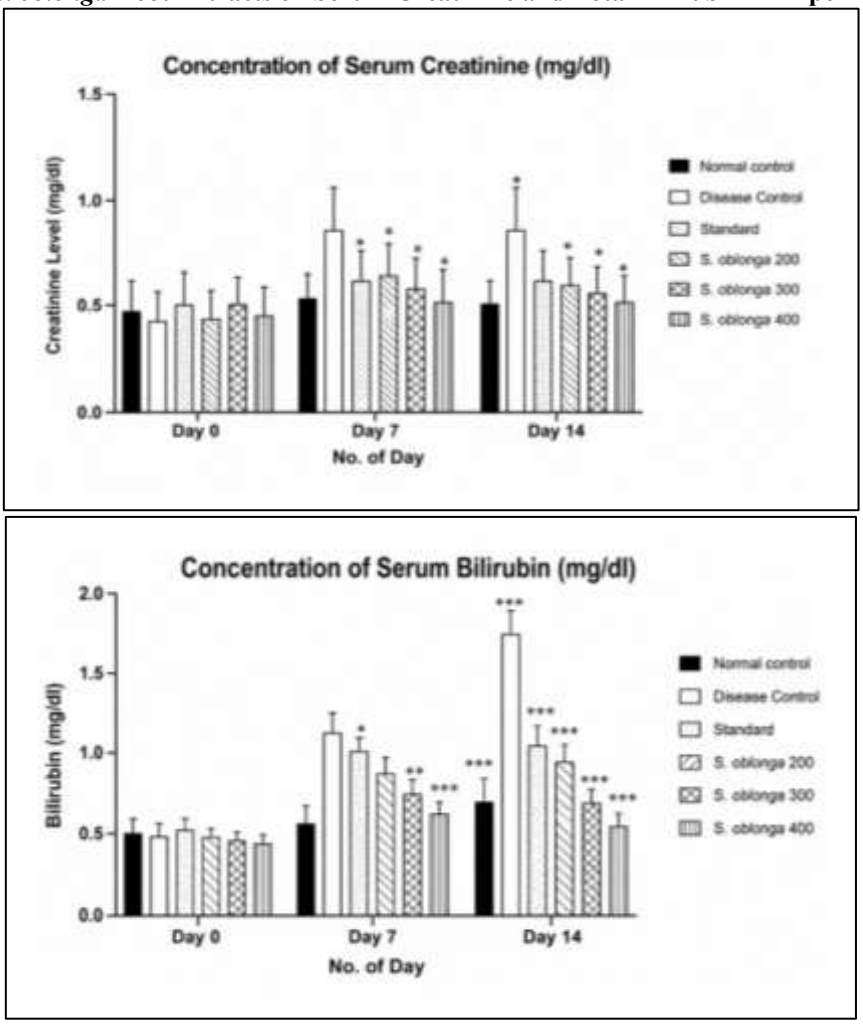
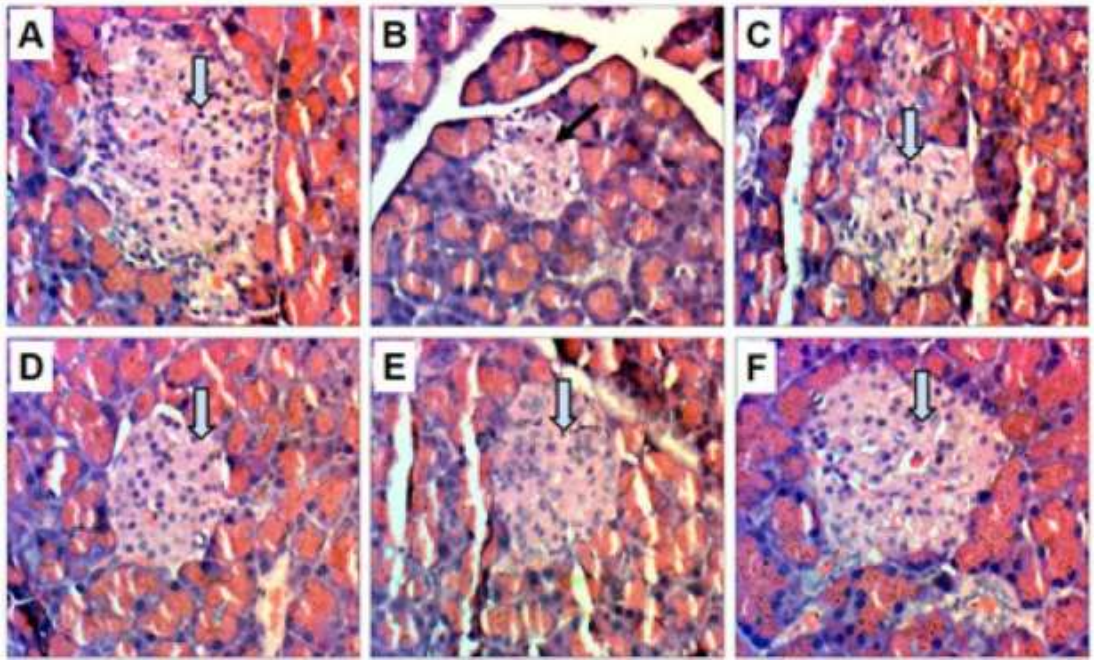


Figure 13: Graph Showing Concentration of Serum Creatinine and Serum Bilirubin (mg/dl) in Different Groups Treated with Root Extracts of *S. oblonga*

3.4.4 Histopathological Analysis



(A) Normal control showing normal islets of Langerhans and intact β-cells. (B) Diabetic control showing shrunken islets, β-cell depletion, necrosis, and inflammatory infiltration. (C) Standard (Metformin, 2 mg/kg) showing restoration of islet architecture and β-cell population. (D) *S. oblonga* 200 mg/kg showing mild regeneration of pancreatic islets. (E) *S. oblonga* 300 mg/kg showing moderate restoration of islet architecture and cellular organization. (F) *S. oblonga* 400 mg/kg showing near-normal islets with marked β-cell regeneration and minimal pathological changes.

4. DISCUSSION:

The present study evaluated the phytochemical composition, antioxidant potential, in vitro antidiabetic activity, and in vivo antihyperglycemic efficacy of *Salacia oblonga* extracts collected from different geographical regions and plant parts. The findings demonstrated that the biological activity of *S. oblonga* varied with geographical origin and plant part, with the root extract from Eleshwaram (SREE) exhibiting the most potent pharmacological effects.

Qualitative phytochemical screening revealed the presence of phenolics, flavonoids, alkaloids, saponins, steroids, and terpenoids in the extracts, while glycosides were absent. SREE contained the highest abundance of bioactive phytochemicals, which correlated with its significantly greater total phenolic content, flavonoid content, and ferric reducing antioxidant power (FRAP). Since phenolic and flavonoid compounds are recognized for their ability to donate electrons, neutralize free radicals, and reduce oxidative stress, their higher concentration in SREE likely contributed to its enhanced antioxidant activity.

The antioxidant assays further confirmed these observations. SREE exhibited superior DPPH, nitric oxide, superoxide, and hydroxyl radical scavenging activities with comparatively lower IC_{50} values than the other extracts, indicating greater free radical scavenging efficiency. Although hydrogen peroxide scavenging activity was comparatively weak in all extracts, SREE consistently showed better activity than SRET and SREK at most concentrations. Similarly, reducing power, phosphomolybdenum, and thiobarbituric acid assays demonstrated concentration-dependent antioxidant activity, with SREE showing the greatest reducing capacity and inhibition of lipid peroxidation. These findings suggest that the antioxidant potential of *S. oblonga* is largely attributable to its rich polyphenolic composition.

Comparison of different plant parts further demonstrated that the root extract possessed markedly higher phenolic, flavonoid, and antioxidant contents than the stem and leaf extracts. The root also showed superior radical scavenging and enzyme inhibitory activities, indicating that it represents the most pharmacologically active part of the plant. These findings support the traditional use of *S. oblonga* roots in the management of diabetes.
The in vitro antidiabetic assays demonstrated effective inhibition of α-glucosidase and α-amylase enzymes by the

root extract. Inhibition of these carbohydrate-hydrolyzing enzymes delays intestinal carbohydrate digestion and glucose absorption, thereby reducing postprandial hyperglycemia. The strong enzyme inhibitory activity observed in SREE is likely associated with the presence of salacinol, kotalanol, phenolics, and flavonoids, which have been reported to inhibit digestive enzymes and improve glycemic control.
Acute toxicity evaluation showed that oral administration of *S. oblonga* root extract up to 2000 mg/kg body weight produced neither mortality nor behavioral abnormalities, confirming its favorable safety profile. This observation indicates a wide therapeutic margin and supports its suitability for further pharmacological evaluation.

In the streptozotocin induced diabetic rat model, administration of *S. oblonga* root extract produced a dose-dependent reduction in both random and postprandial blood glucose levels throughout the treatment period. The 400 mg/kg dose showed the greatest antihyperglycemic effect, which was comparable to the standard drug Metformin by day 14. Furthermore, treatment improved lipid abnormalities by reducing total cholesterol and triglycerides while maintaining HDL-cholesterol levels. Serum creatinine and bilirubin levels also approached normal values, indicating protection against diabetes-associated renal and hepatic dysfunction. Histopathological examination further demonstrated regeneration of pancreatic islets, restoration of β-cell architecture, and reduced inflammatory changes in extract-treated groups, particularly at 400 mg/kg, confirming the protective effect of *S. oblonga* against STZ-induced pancreatic injury.

Overall, the results indicate that the antidiabetic activity of *S. oblonga* is mediated through multiple mechanisms, including potent antioxidant activity, inhibition of carbohydrate-hydrolyzing enzymes, improvement of glucose homeostasis, correction of dyslipidemia, protection of vital organs, and preservation of pancreatic β-cell integrity. These complementary mechanisms support the therapeutic potential of *S. oblonga* as a promising natural antidiabetic agent.

5. CONCLUSION

The present study demonstrated that *Salacia oblonga*, particularly the root extract collected from Eleshwaram, possesses significant antioxidant and antidiabetic activities. The root extract contained the highest levels of phenolics and flavonoids and exhibited superior free radical scavenging capacity, reducing power, and inhibition of α-glucosidase and α-amylase compared with extracts from other geographical regions and plant parts. The extract was found to be safe up to 2000 mg/kg body weight and produced dose-dependent antihyperglycemic effects in streptozotocin induced diabetic rats. Treatment also improved lipid profile, reduced serum creatinine and bilirubin levels, and restored normal pancreatic histoarchitecture, with the 400 mg/kg dose showing efficacy comparable to metformin. Collectively, these findings suggest that *S. oblonga* root extract is a promising source of bioactive compounds with multitarget antidiabetic potential and warrants further investigation for isolation of active constituents and clinical development as a safe phytotherapeutic agent for the management of type 2 diabetes mellitus.

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