Evaluation of Anti-Diabetic Activity of Methanolic Extract of *Costus pictus* in STZ-Induced Diabetic Sprague Dawley Rats

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Abstract

This study investigated the anti-diabetic properties of the methanolic extract of *Costus pictus* rhizomes, a plant traditionally recognized for its role in diabetes management, using streptozotocin-induced diabetic Sprague Dawley rats as the experimental model. A total of 42 SD/NIN male rats were categorized into following four groups: a control group (Normal without disease induction or treatment), a diabetic control group, and two treatment groups receiving *Costus pictus* extract at oral doses of 50 mg/kg and 250 mg/kg body weight through gavaging. Over a four-week treatment period, key indicators such as body weight, blood glucose levels, biochemical markers were thoroughly evaluated.

The results revealed a dose-dependent reduction in blood glucose levels, with the 250 mg/kg dose achieving a 52% reduction by the fourth week, compared to 49.5% at 50 mg/kg. Treated groups also exhibited improved lipid profiles, liver enzyme levels, and kidney function markers compared to diabetic controls. Histopathological analysis showed significant β-cell regeneration in treated groups, particularly at the higher dose, indicating the potential of *Costus pictus* to restore pancreatic function.

This study highlights the therapeutic efficacy of *Costus pictus* in managing hyperglycaemia and mitigating metabolic dysfunctions associated with diabetes. The plant's antioxidant and anti-inflammatory properties likely contribute to its beneficial effects, making it a promising alternative to synthetic anti-diabetic agents. While the results are encouraging, further studies are needed to understand the detailed mechanisms of action, optimize dosing, and evaluate clinical efficacy in humans. These findings reinforce the potential of *Costus pictus* as a cost-effective and natural remedy for diabetes and its complication management.

Introduction

Diabetes mellitus, a metabolic disorder of hyperglycaemia seen as chronic ailment emerged as a global health challenge, affecting millions worldwide [1]. The prevalence of diabetes in the world has been increasing exponentially[2], while we are witnessing the various forms of diabetes in the society[3], underscoring the urgent need for effective management strategies to address its complications and reduce its public health burden. The consequences of poorly managed diabetes extend beyond elevated blood sugar levels, as chronic hyperglycaemia significantly contributes to micro as well as macrovascular complications[4, 5]. These complications not only impair the quality of life of individuals but also place a considerable economic strain on healthcare systems. Despite advancements in pharmacological treatments, the limitations of synthetic drugs, such as adverse side effects, high costs, and poor patient compliance, have necessitated the exploration of alternative therapeutic approaches.

Medicinal plants have gained considerable attention for their therapeutic potential, safety, and affordability in managing diabetes. Traditional medicine systems around the world have relied on plant-based remedies, many of which have shown promising results in controlling hyperglycaemia [6–8]. One such plant, *Costus pictus*, commonly referred to as the insulin plant [9], has been traditionally used to

manage diabetes, particularly in regions like Kerala, India. Belonging to the family *Costaceae*, *Costus pictus* contains bioactive compounds, including diosgenin [10], which is a precursor for the synthesis of various pharmaceutical drugs. Given the increasing prevalence of diabetes and the limitations of conventional therapies, *Costus pictus* presents a promising herbal alternative due to its safety, affordability, and cultural acceptability [11]. Additionally, studies have demonstrated that *Costus pictus* possesses significant anti-inflammatory and antioxidant properties, which help alleviate oxidative stress and chronic inflammation commonly linked to diabetes and its associated complications[12, 13]. These multifaceted effects make *Costus pictus* a compelling candidate for further exploration in diabetes management.

This study aims to evaluate the anti-diabetic (anti-hyperglycaemia) activity of the methanol-based extract of *Costus pictus* in SID Sprague Dawley rats. The objectives include the collection and preparation of methanolic extracts of *Costus pictus* rhizomes and their evaluation for anti-diabetic potential in diabetic rats.

Materials and Methods

Study Design

The study was conducted to evaluate the anti-diabetic activity of the methanol-based extract of *Costus pictus* rhizomes in a streptozotocin-induced diabetic (SID) rat model. Ethical approval for the experimental protocol was obtained from the local (Institutional) Animal Ethics Committee (ICMR-NIN Animal Ethics number: P10F/IAEC/NIN/2017/MSV/SD) prior to commencement. A total of 42 Sprague Dawley adult male (11–12 weeks old) rats were used for the study and were randomly allotted into four groups (Fig. 1). Group 1 served as the normal control, consisting of non-diabetic rats (n = 8), maintained without any induction of diabetes or treatment. Group 2 comprised diabetic control rats (n = 12), which were induced with STZ to develop diabetes but received no further treatment. Groups 3 and 4 included diabetic rats treated with *Costus pictus* extract at two different doses: Group 3 received a low dose of 50mg/kg body weight (n = 12), while Group 4 was administered a high dose of 250mg/kg body weight (n = 12). The methanolic extract was administered daily to test groups (3 and 4) through oral gavaging (0.5ml/animal) for a period of six weeks daily. This design allowed for the assessment of the dose-dependent effects of the extract on diabetic parameters. Each group was carefully monitored throughout the study period to evaluate the therapeutic efficacy and safety of the *Costus pictus* extract.

Plant Botanical and Morphological Information (Fig. 2)

Costus pictus D. Don, widely recognized as spiral ginger or the insulin plant, belongs to the family Costaceae. It is a perennial rhizomatous herb valued for its extensive medicinal applications, particularly in traditional systems of medicine for managing diabetes and related metabolic conditions. The plant is characterized by sub-sessile leaves that are elliptic to obovate in shape, providing a lush, green

appearance. The inflorescence appears as prominent spikes with large bracts positioned sub-terminally, adding to its distinct morphology. The flowers are vibrant, with their size ranging between 5–6 cm in length, and exhibit a cup-shaped labellum with a yellow crest bearing intricate lines, enhancing their ornamental and botanical significance.

The fruits of Costus pictus are capsular in structure, containing five black seeds encased in a fleshy white aril, which supports the plant's reproductive efficiency. The rhizomes, a critical component of the plant, serve as a rich source of bioactive compounds, including diosgenin (a steroidal sapogenin), tigogenin, dioscin, gracillin, and β-sitosterol glucoside. These phytochemicals contribute to its diverse pharmacological properties, such as antidiabetic, antihyperglycemic, astringent, and expectorant activities. The rhizomes also play a significant role in traditional treatments for jaundice, pneumonia, rheumatism, constipation, and diarrhoea, reflecting the plant's versatility in therapeutic applications.

Due to the high demand for diosgenin in pharmaceutical formulations, Costus pictus is often overharvested, leading to its depletion from natural habitats. The plant's unique morphology and extensive medicinal potential underscore its significance as a valuable resource in biomedical research, particularly in studies focused on diabetes and metabolic disorders. This study utilizes the rhizomes of Costus pictus to explore its efficacy in managing SID in a rat model, highlighting the relevance of this plant in modern pharmacological investigations.

Plant Material Collection and Preparation

The rhizomes of *Costus pictus* were collected from various regions and authenticated by experts at Osmania University. The plant material was carefully rinsed with flowing tap water, allowed to air dry completely, and then ground into a coarse powder. Approximately 200 g of the powdered rhizomes were subjected to Soxhlet extraction using methanol as the solvent. The methanolic extract was concentrated under reduced pressure using a rotary evaporator, yielding a semisolid residue. The residue was weighed and stored at 4°C for further analysis and use. For administration, the extract was dissolved in a 1% Tween 80 solution to prepare the desired doses.

Animal Housing and Maintenance

The rats were procured from the National Centre for Laboratory Animal Sciences (currently named as ICMR-NIN Animal Facility) and housed in standard laboratory conditions. The animals were kept in individual cages under a controlled environment (temperature @22 ± 2°C and relative humidity 45–55%, and a 12-hour light/dark cycle). A standard stock diet and water were provided *ad libitum* throughout the study. The rats were acclimatised for one week before initiating the experiments.

Induction of Diabetes

Diabetes in SD rats was induced in three groups (2, 3, & 4) by a single intraperitoneal (i/p) injection of streptozotocin (STZ @ 37 mg/kg body weight) dissolved in citrate buffer (pH 4.5). After 72 hours, blood glucose levels were measured at five time-points using a glucometer (Accu-Chek, Roche Diabetes Care India Private Limited), and rats with fasting blood glucose levels of 200 mg/dL or higher were considered diabetic and included in the study.

Experimental Protocol

The treatment period spanned six weeks, during which several parameters were systematically monitored to evaluate the effects of diabetes and *Costus pictus* extract treatment. Blood glucose levels were measured weekly by collecting blood samples via retro-orbital sinus puncture under mild anaesthesia(isoflurane), using a glucometer for analysis. Body weight was recorded weekly for each rat to assess the physical impact of diabetes and treatment. Additionally, daily food intake was carefully measured to identify any changes associated with metabolic alterations.

At the conclusion of the six-week period, the rats were fasted overnight, and final blood samples were collected for a detailed biochemical analysis. Subsequently, the animals were euthanized using humane method using CO_2 asphyxiation, and tissues were harvested for histopathological evaluation.

Plasma samples were analysed using an autoanalyzer (Cobos c 311 analyser, Roche) to assess key biochemical parameters. These included the lipid profile (total cholesterol and triglycerides) to evaluate metabolic disturbances, and liver and renal function tests, such as alanine transaminase (SGPT), aspartate transaminase (SGOT), alkaline phosphatase (ALP), bilirubin, creatinine, and urea, to determine the systemic effects of the treatment. Additionally, other parameters, such as total protein and albumin levels, were measured to provide insights into overall metabolic health and protein metabolism. This comprehensive analysis aimed to elucidate the therapeutic effects of *Costus pictus* on both metabolic and systemic health in the diabetic rat model.

Histopathological Evaluation

The pancreas, liver, kidneys, and spleen were dissected, fixed in 10% formalin, and processed for histopathological analysis. Sections were stained with haematoxylin and eosin stains to examine structural changes and assess any regenerative effects of *Costus pictus* extract on pancreatic β-cells.

Statistical Analysis

Statistical analysis was conducted to comprehensively evaluate the anti-diabetic potential of *Costus pictus* methanolic extract and its impact on biochemical, physical, and gross morphology of visceral organs in an STZ-induced diabetic rat model. Data were expressed as mean ± standard deviation (SD) whereas statistical significance was assessed using SPSS software (version 20). A one-way ANOVA was employed to compare the means of various parameters across groups, followed by Tukey's post-hoc test

for pairwise comparisons. Changes within each group before and after treatment were analysed using paired t-tests. The respective p-value < 0.05 was considered statistically significant, ensuring robust and reliable interpretation of the results.

Results

Effect of Costus pictus on Blood Glucose Levels (Table 1a and Table 1b)

Blood glucose levels were monitored weekly for four weeks to evaluate the anti-diabetic potential of *Costus pictus*. A significant reduction in blood glucose levels was observed in the treated groups (Group 3: 50 mg/kg and Group 4: 250 mg/kg) compared to the diabetic control group (Group 2). The most pronounced reduction was seen in Group 4, which exhibited a 52% decrease in glucose levels by the end of the fourth week. Group 3 showed a reduction of 49.5%, highlighting the dose-dependent effect of the extract. The statistical analysis using a paired t-test revealed a significant reduction ($p < 0.05$) in blood glucose levels in both treated groups compared to the diabetic control group.

Effect on Body Weight and Biochemical Parameters (Table 2a and Table 2b)

The body weight of the animals was monitored weekly to evaluate the physical impact of diabetes and the effect of *Costus pictus* extract treatment. Group 2, the diabetic control group, exhibited a significant reduction in body weight over the study period, with a decrease of 18.4% from an initial weight of 247.2 ± 3.6 g to 201.6 ± 6.7 g by the fourth week. In contrast, treated groups demonstrated a slower rate of weight loss. Group 3, receiving 50 mg/kg of *Costus pictus*, experienced a 22.1% decrease from 249.5 ± 4.7 g to 194.4 ± 5.9 g, while Group 4, treated with 250 mg/kg, showed a 20.8% reduction from 250.6 ± 5.3 g to 198.4 ± 6.9 g. Notably, Group 1, the normal control group, maintained stable body weights, with a slight increase of 4.2% from 253.3 ± 5.6 g to 263.9 ± 5.9 g, reflecting overall metabolic stability and health. These observations suggest a dose-dependent effect of *Costus pictus* in mitigating weight loss typically associated with diabetes.

The administration of *Costus pictus* extract also improved key biochemical markers in diabetic rats. Lipid profiles showed moderate reductions in triglycerides and cholesterol levels in treated groups compared to the diabetic control. Group 3 recorded triglyceride levels of 34.9 ± 9.8 mg/dL and Group 4 at 39.3 ± 8.5 mg/dL, compared to 42.5 ± 5.4 mg/dL in Group 2. Similarly, liver function tests revealed reduced levels of SGOT, SGPT, and ALP in treated groups. For instance, Group 3 and Group 4 recorded SGPT levels of 126.8 ± 19.2 µu/dL and 143.4 ± 11.1 µu/dL, respectively, compared to 113.6 ± 11.3 µu/dL in the diabetic control. ALP levels were significantly elevated in Group 4 (410 ± 31 µu/dL) relative to 293 ± 40 µu/dL in Group 3 and 307 ± 39 µu/dL in Group 2, suggesting an overall protective effect on liver health.

Kidney function tests further reflected marginal improvements, with reduced urea and creatinine levels in treated groups compared to the diabetic control. Total protein levels in treated groups remained closer to those of the normal control, indicating preserved protein metabolism. Group 3 and Group 4 maintained glucose levels at 158.11 ± 17.68 mg/dL and 166.44 ± 38.74 mg/dL, respectively, compared to 315.89 ± 26.96 mg/dL in the diabetic control, further underscoring the extract's efficacy in reducing hyperglycaemia and improving overall metabolic health. These findings suggest that *Costus pictus* extract exerts a significant protective effect on metabolic and organ function in diabetic rats.

Food Intake (Table 3)

Food intake patterns were monitored to assess metabolic changes during treatment. Group 4 exhibited a slight increase in food intake compared to control (2%), possibly reflecting improved metabolic efficiency. In contrast, no significant changes were observed in Groups 2 and 3 compared to baseline.

Significant differences in blood glucose levels were observed between the diabetic control group and the treated groups, with Group 4, receiving the higher dose of *Costus pictus* extract, exhibiting the most pronounced reduction ($p < 0.05$). Similarly, body weight analysis showed significant differences between the diabetic control and treated groups, with both treatment doses mitigating the weight loss typically observed in diabetic conditions ($p < 0.05$). Biochemical parameters, including lipid profiles and liver enzyme levels, also showed significant improvement in the treated groups compared to the diabetic control group ($p < 0.05$). Histopathological evaluation further corroborated these findings, revealing consistent regeneration of pancreatic β-cells in treated groups, with the highest dose (Group 4) demonstrating superior restorative effects compared to the lower dose (Group 3).

These results underscore the efficacy of *Costus pictus* methanolic extract as a potent anti-diabetic agent. The extract not only ameliorated hyperglycaemia but also improved metabolic parameters and anatomical outcomes, highlighting its potential to address the biochemical and structural abnormalities associated with diabetes.

Histopathological Analysis (Table 4)

Histopathological examination of pancreatic tissues revealed significant restoration of β-cell architecture in the treated groups compared to the diabetic control group. Group 4 (250 mg/kg) demonstrated marked improvement, with reduced cellular degeneration and increased β-cell mass. Group 3 (50 mg/kg) also showed moderate regeneration, though less pronounced than Group 4. The diabetic control group exhibited extensive damage, including necrosis and loss of β-cell integrity.

Discussion

The current study highlights the significant anti-diabetic potential of *Costus pictus* methanolic rhizome extract, with a 52% reduction in blood glucose levels observed at a 250 mg/kg dose, alongside marked improvements in lipid profiles, liver enzyme levels, and pancreatic β-cell regeneration. These findings align with previous research emphasizing the therapeutic value of traditional medicinal plants in diabetes

management [10, 14, 15]. However, the current study adds depth by focusing on the dose-dependent effects of the rhizome extract, offering unique insights into its systemic metabolic benefits. The ability of *C. pictus* to significantly reduce glucose levels is likely attributed to bioactive compounds such as diosgenin, known to enhance glucose uptake and suppress hepatic glucose production, as reported in similar studies [16]. This positions *C. pictus* as a promising alternative for populations seeking natural remedies for diabetes.

Body weight trends in the study further underscore the protective role of *C. pictus* against diabetes-induced catabolism. Diabetic control rats exhibited significant weight loss, a hallmark of uncontrolled diabetes, while treated groups, particularly at the higher dose, showed slower weight decline. This stabilization may be linked to the extract's ability to restore metabolic homeostasis and reduce muscle protein breakdown. These observations, combined with the hypoglycaemic effects, suggest that *C. pictus* not only regulates glucose but also mitigates broader metabolic disruptions caused by diabetes.

The biochemical parameters analysed in this study offer additional insights into the extract's therapeutic potential. Elevated triglycerides and cholesterol levels, characteristic of diabetic dyslipidaemia, were reduced in the treated groups, reflecting the lipid-lowering effects of the extract. This aligns with its antioxidant properties, which likely counteract oxidative stress and inflammation—key contributors to dyslipidaemia in diabetes. Moreover, the observed reductions in liver enzymes (SGOT, SGPT, and ALP) highlight the hepatoprotective role of the extract. By mitigating hepatic damage, *C. pictus* not only aids in glucose regulation but also addresses one of the critical complications of diabetes, expanding its therapeutic scope.

Histopathological examination provided compelling evidence of pancreatic β-cell restoration in the treated groups. Diabetic control rats exhibited significant degeneration and necrosis of β-cells, consistent with the cytotoxic effects of STZ. In contrast, the higher dose of *C. pictus* extract demonstrated significant regeneration of β-cell architecture, with increased cellular integrity and mass. This suggests that *C. pictus* not only manages hyperglycaemia but also targets the underlying pathology of diabetes—insulin deficiency due to β-cell loss. The moderate improvements seen in the lower-dose group reinforce the importance of dose optimization for maximizing therapeutic efficacy.

Food intake patterns remained stable across groups, with a slight increase observed in the high-dose treated group. This could indicate improved metabolic efficiency and reduced energy wastage, a common feature of uncontrolled diabetes. The stable feeding behaviour also underscores the tolerability of the extract, positioning it as a potentially safe intervention for long-term use. These observations align with previous studies that emphasize the multi-targeted effects of natural compounds in diabetes management [17, 18].

When compared to earlier studies, the findings of the current study extend our understanding of *C. pictus*. For instance, Jayasri et al. (2008) demonstrated the glucose-lowering effects of *C. pictus* leaf extract in STZ-induced diabetic rats[17], while the current study highlights the broader systemic recovery

achieved through rhizome extracts. Similarly, Bhuyan et al. (2019) identified specific bioactive flavanones in methanolic extracts that contributed to anti-diabetic effects[18], while this study provides evidence for dose-dependent systemic benefits, particularly in lipid metabolism and β-cell regeneration.

Other studies further emphasize the multi-functional properties of *C. pictus*, including its anti-inflammatory, antimicrobial, and anticancer activities[12, 19]. The current study aligns with these findings, particularly by showcasing the rhizome extract's dual role in managing diabetes and improving hepatic and pancreatic functions. Molecular insights from Annadurai et al. (2012) and Nevin et al. (2021) also complement the current study, highlighting pathways such as GLUT-2 upregulation and enzyme inhibition as mechanisms underlying the plant's anti-diabetic effects[20, 21]. These mechanistic findings align with the systemic outcomes observed in this study, collectively emphasizing the therapeutic promise of *C. pictus*.

The comparative insights with studies by Jothivel et al. (2007) and Gireesh et al. (2009) demonstrate that while leaf extracts exhibit significant glucose-lowering effects, rhizome extracts provide enhanced systemic and anatomical recovery, particularly at higher doses[22, 23]. The phytochemical profiling of *C. pictus* by Shiny et al. (2013) also supports these findings [24], suggesting that both leaves and rhizomes contain bioactive compounds with therapeutic potential.

Furthermore, advancements in sustainable cultivation methods, such as those discussed by Punyarani et al. (2012), align with the findings of this study by ensuring the long-term availability of *C. pictus* for therapeutic applications[25]. This integration of cultivation strategies with pharmacological insights ensures that *C. pictus* can serve as a reliable source for pharmaceutical development.

In conclusion, the current study consolidates and extends the existing body of evidence on *Costus pictus*, highlighting its systemic anti-diabetic potential through comprehensive biochemical, anatomical, and dose-response evaluations. By bridging traditional knowledge with scientific validation, *C. pictus* emerges as a versatile and promising candidate for managing diabetes and associated metabolic disorders, paving the way for future clinical applications. These findings also underscore the need for further research into its molecular mechanisms, long-term efficacy, and potential for standardization as a nutraceutical or pharmaceutical agent.

Conclusion

The findings of this study demonstrate the significant anti-diabetic potential of the methanolic extract of *Costus pictus* rhizomes in STZ-induced diabetic Sprague Dawley rats. The extract exhibited a dose-dependent reduction in blood glucose levels, with the higher dose (250 mg/kg) achieving a remarkable 52% reduction by the end of four weeks. Additionally, improvements in lipid profiles, liver and kidney function markers, and the preservation of body weight highlight its multi-targeted therapeutic effects. Histopathological analysis further revealed the restorative effects of *Costus pictus* on pancreatic β-cell

architecture, suggesting its potential to address the underlying pathology of diabetes rather than merely managing hyperglycaemia.

The observed improvements in metabolic parameters, combined with the absence of significant adverse effects, position *Costus pictus* as a promising natural alternative to synthetic anti-diabetic agents. Its antioxidant and anti-inflammatory properties likely contribute to its efficacy, offering a holistic approach to diabetes management by addressing oxidative stress and inflammation, which are key contributors to the progression of diabetic complications.

While the results are encouraging, further research is required to establish the long-term efficacy, optimal dosing, and precise mechanisms of action of *Costus pictus*. Future studies should also explore its clinical applicability and safety in human populations. This study bridges traditional medicinal knowledge and scientific validation, paving the way for *Costus pictus* to be considered a cost-effective and accessible intervention in diabetes management. If successfully translated into clinical practice, this plant-based remedy has the potential to significantly alleviate the global burden of diabetes and improve the quality of life for millions of affected individuals.

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Tables

Tables 1 to 4 are available in the Supplementary Files section.

Figures

Figure 1: Study Design for Evaluating the Effects of *Costus pictus* in a Streptozotocin (STZ)-Induced Diabetes Model

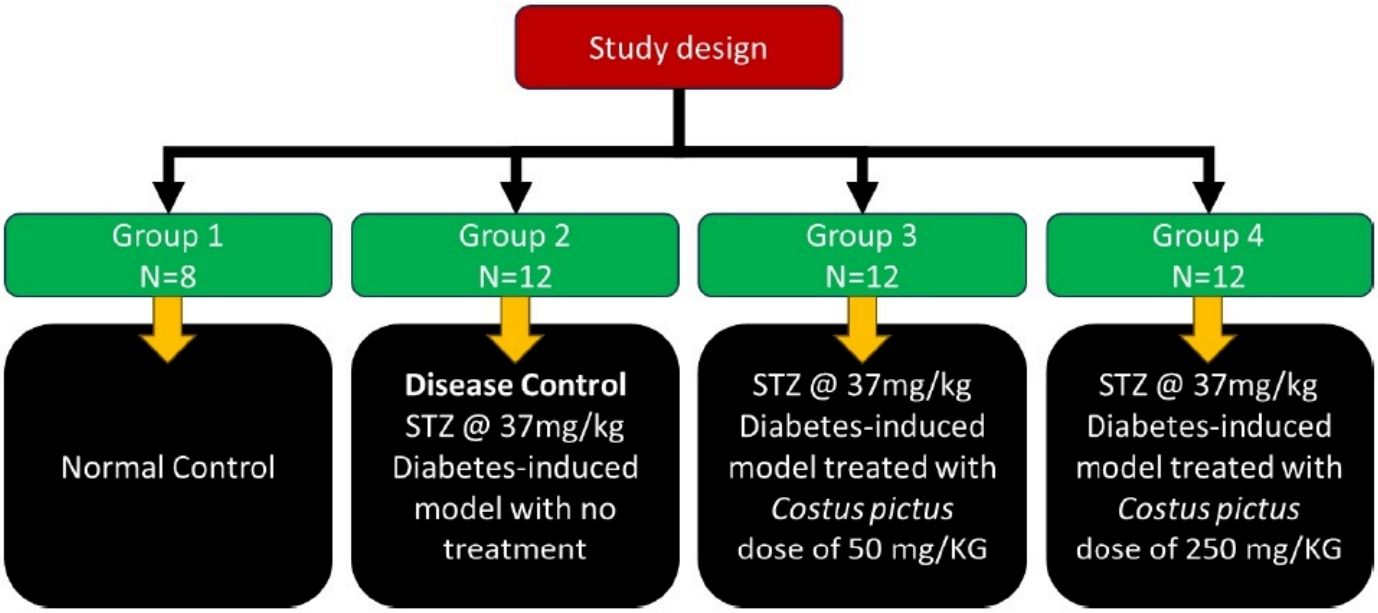

Figure 1

See image above for figure legend

Figure 2: Botanical information of *Costus pictus* used in this study

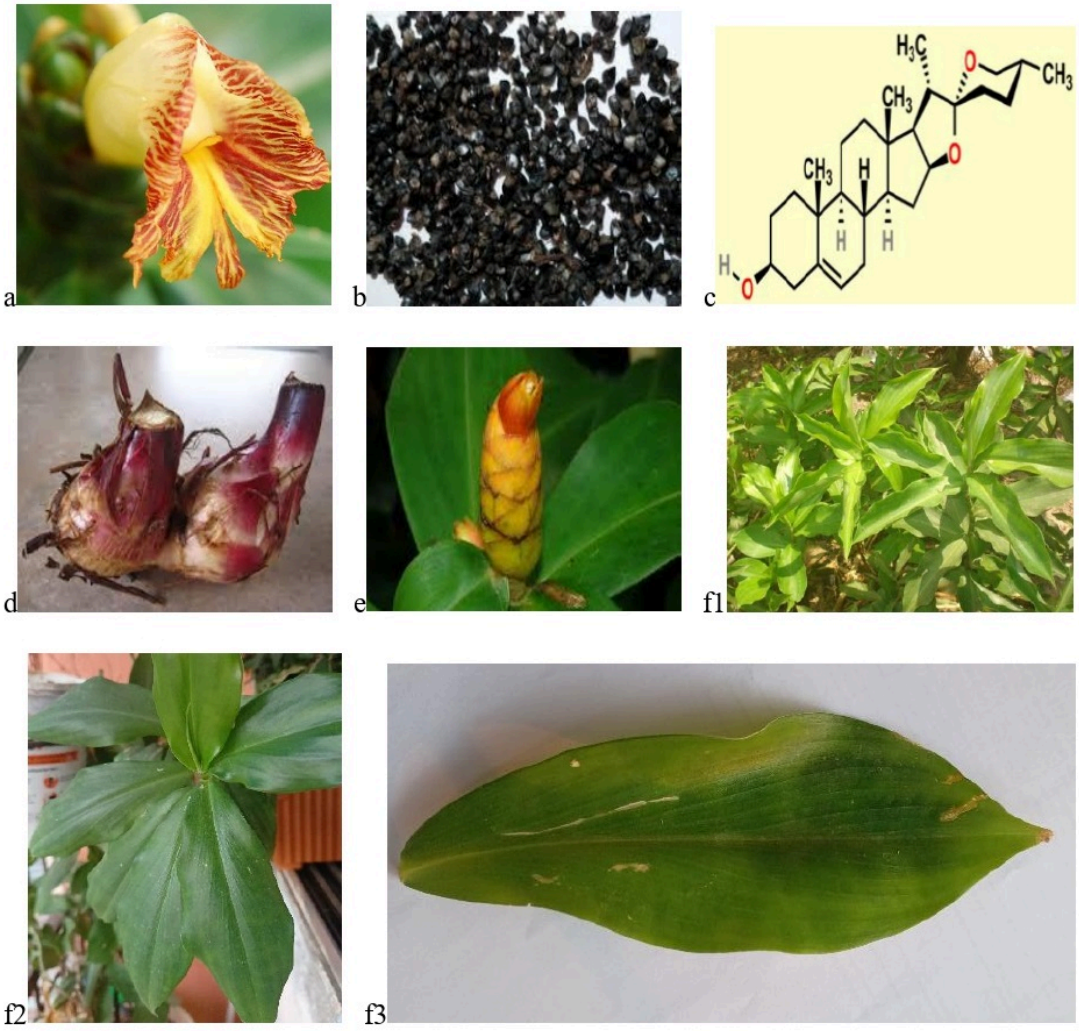

Figure 2 provides detailed botanical information on *Costus pictus* used in this study. Panel (a) shows the vibrant flower of *Costus pictus*, characterized by its yellow hue and striking red streaks. Panel (b) highlights the small, dark, and textured seeds of the plant, indicative of its reproductive mechanism. Panel (c) presents the chemical structure of a bioactive compound, likely representing a steroidal or medicinal molecule derived from *Costus pictus*. Panel (d) displays the thick, reddish-purple rhizomes, showcasing the plant's underground parts. Panel (e) depicts a cone-like bud in its early blooming stage with an orange-yellow color. Panels (f1) and (f2) illustrate the dense green foliage and mature broad leaves with a smooth texture, respectively. Lastly, panel (f3) focuses on a single lanceolate-shaped leaf, highlighting its visible veins and natural wear patterns.

Figure 2

See image above for figure legend

Supplementary Files

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- Table1a.jpg
- Table1b.jpg
- Table2a.jpg
- Table2b.jpg
- Table3.jpg
- Table4.jpg