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ANTIHYPERGLYCEMIC ACTIVITY OF A FLOUR MIX PREPARATION FROM *Amorphophalus campanulatus* (ELEPHANT FOOT YAM) AGAINST STREPTOZOTOCIN – NICOTINAMIDE INDUCED DIABETIC WISTAR RATS

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ABSTRACT

Elephant foot yam (*Amorphophallus campanulatus*) is a tropical tuber with significant nutritional and medicinal potential but is underutilized due to its anti-nutritional factors. This study evaluated the anti-hyperglycaemic effects of resistant starch (RS) derived from *A. campanulatus* in streptozotocin - nicotinamide (STZ-NIC) induced diabetic Wistar rats. RS was prepared by autoclaving, retrogradation, and enzymatic hydrolysis. Acute confirmed safety up to 2000 mg kg^{-1}. Diabetic rats treated with RS @ 100 and 200 mg kg^{-1} for 28 days exhibited significant reduction in fasting blood glucose. The blood glucose level in the diabetic control group on day first was 284.8 ±6.1 mg dL^{-1} and on day 28 was 293.2 ± 6.5 mg dL^{-1}. HbA1c, urea, and creatinine, alongside increased in plasma insulin, liver glycogen, total protein, and body weight, comparable to glibenclamide. Histopathological analysis showed β-cell preservation in RS-treated groups. Additionally, RS promoted the growth of beneficial gut microbiota, reinforcing its prebiotic role. These findings indicated that RS from *A. campanulatus* holds promise as a functional food ingredient with anti-diabetic and gut-modulatory benefits.

Keywords: Elephant foot yam, functional food, gut microbiota, glycemic control, plasma insulin, type-2 diabetes

INTRODUCTION

The king of tuber crop, elephant foot yam (*Amorphophalus campanulatus*), commonly called ‘Oal or Jimikand/ Suran’ in India, is a tropical aroid tuber vegetable crop and finds its application in most of the Indian medical systems such as Ayurveda, Siddha and Unani. It reportedly is a natural probiotic that protect gut microflora and fauna with deliberately low fat in content and rich in omega-3-fatty acids (Jogi and Lahre, 2020). But conversely the presence of anti-nutritional factors such as Raphides that are needle-like oxalate crystals that cause acridity so renders it underutilized by major consumers

(Hosseini *et al.,* 2015; Srivastava *et al.,* 2022). The polysaccharides of yam-based products are potentially viable medicinal because of bioactivities such as immune regulatory, anti-tumour activity, anti-hypoglycemic, etc. The gut microbiota such as *Bifidobacteria* and *Lactobacillus* show increase upon the consumption of non-starch polysaccharides of yam products, more particularly the resistant starch acts as a prebiotic compound that facilitate the liberation of short chain fatty acids (SCFA) like butyric and propionic acids (Srivastava *et al.,* 2022). SCFA helps to improve digestion in the large intestine and lower the plasma cholesterol in tested rats. These oxalate crystals cause irritable mouth feel and itching in hands during processing and in throat and mouth when consumed without a proper pretreatment. Other anti-nutritional factors include tannins, phytic acids, hydrogen cyanides that cause intoxication in milch animals, causing ephemerality or lowered feed intake. With appropriate cooking and processing methodologies, the toxic factors and the anti-nutritional elements could be eliminated.

Diabetes mellitus is one of the most common disorders affecting about 6% world population and the dynamics of diabetes is changing rapidly in low to middle income countries. As per International Diabetes Federation's (IDF) estimates 80% world diabetic population are from low- and middle-income countries (Gong *et al.,* 2022). Diabetes usually develops due to deficiency of insulin secretion or may be also due to the diminished expectancy of the patients. Several plant-based medicines have been practiced for the management of different diseases in Asian countries as well as in other parts of the world (Kumar, *et al*., 2017). However, the exact mechanisms of mode of action of this plant-based food preparation are not well studied. Currently, evaluation of the use of different herbal preparation for treating various diseases including diabetes is emphasized (Sharma *et al.,* 2020).

The use of probiotics in commercial formulations of lactic acid bacteria for enhancing the probiotic population during the treatment of digestive disorders and additionally it offers fruitful improvement in gut health. The population of *Lactobacillus bulgaricus* was observed over 28 days which revealed some significant results regarding the possible attribute of resistant starch as prebiotic effect on retaining the cell viability. The results indicate that *L. bulgaricus* was higher in resistant starch containing sample and was significantly higher than that of glucose and inulin (Choudhury *et al.,* 2017). The final count of *L. bulgaricus* was 1.5 log units lower than the count in the media amended with inulin which infers that RS addition acts as prebiotic during the period and maintains cell viability throughout fermentation period to influence the growth. The stimulating effect of probiotics by inulin has been established, and microbial counts in pure cultures of *L. bulgaricus, L. rhamnosus, L. acidophilous, Bifidobacterium* sp., *Streptococcus thermophilous* (Pereira *et al.,* 2023). The effect of inulin in skim milk fermented with *L. bulgaricus, L. rhamnosus, L. acidophilous, Bifidobacterium, Streptococcus thermophilous* was proved to increase the population of LAB over period. Growth kinetics of *L. bulgaricus* was studied in presence of 4 g inulin per 100 g media. Supplementation of inulin lowered the generation time for *L. bulgaricus* by initiating the prebiotic effect of inulin and RS. The prebiotic studies on yoghurt cultures such as *L. bulgaricus*, and *S. thermophilous* also coincides the results of present study of EFY RS. (De Souza Oliveira *et al.,* 2010)

The search for new prebiotics that may act as polysaccharide/biopolymer carriers for probiotics appear relatively promising. There are a few reports on prebiotics like β-glucan, vegetable protein hydrolysate, liquid sea weed extract, standard inulin, long chain inulin, galacto-oligosaccharide, raffinose, snow crab-derived chitooligosaccharide, saccharicterpenin, mannan oligosaccharide, astralagus polysaccharide, *Lentinus*, etc. that originate from plants and play multiple role in functional food that act as prebiotic and anti-diabetic (Akhavan *et al.,* 2023). The perusal of literature suggests that the treatment of rats with streptozotocin alone damages pancreatic β-cells resulting in inadequate production of insulin, and thereby these animals manifest with type 1 diabetes. However, nicotinamide partly protects β-cells of pancreas *via* nitric oxide-mediated mechanisms, and thereby partly preserves the pancreatic β-cells. Therefore, the rats are treated with nicotinamide/streptozotocin to produce type 2 diabetes (Szkudelski, 2012). Consequently, the current study was aimed to explore the potential mechanisms by which the resistant-starch from elephant foot yam (*Amorphophalus campanulatus*) protects against streptozotocin nicotinamide induced type 2 DM in rats.

MATERIALS AND METHODS

Selection of animals

Adult Wistar rats (180 ± 10 g weight; 6-20 weeks-age) of either sex were obtained from animal house, K.M. College of Pharmacy, Madurai (India). The animals were housed in large, spacious polyacrylic cages at ambient temperature with 12-h light/12-h dark cycle. Rats had free access to water and rodent pellets diet (Hindustan Lever, Bangalore, India). The present study was approved by the Institutional Animal Ethics Committee of K.M. College of Pharmacy (approval No. IAEC/Dr. K. Jothilakshmi/ TNAU/ UP17GPT9770007/KMCP/182023-24). All the experiments were carried out in adherence to guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals.

Preparation of elephant foot yam starch

Autoclaving-cooling (AC) modification improved the resistant starch, according to methods used. Starch was isolated by grinding the elephant foot yam (EFY) tubers and autoclaved at 120°C, followed by retrogradation cycles to produce resistant starch. The RS was further hydrolysed using α-amylase and amyloglucosidase. *L. bulgaricus,* obtained from NDRI, Bangalore (India), was activated, grown in media containing RS and hydrolysed RS, and growth was assessed via optical density and pH. The relative prebiotic efficacy was quantified by measuring probiotic proliferation, indicating the prebiotic potential of RS of EFY (Putra, 2020; Li *et al.,* 2018).

Acute oral toxicity

Acute oral toxicity of resistant starch of *A. campanulatus* was carried out as per the guidelines of the Organization for Economic Co-operation and Development (OECD) [revised draft guidelines 423]. (Parasuraman, 2011). It involves a stepwise procedure with the use of minimum number of animals per step to obtain sufficient information on acute toxicity of test substance to enable its classification. Healthy Wistar rats (3 animals/dose) of either sex were used in the experiment. Overnight fasted rats were orally fed with above resistant starch in increasing dose levels of 300 and 2000 mg kg^{-1} body weight, respectively. The animals were observed for their behavioural (alertness, restlessness, irritability and fearfulness), neurological (spontaneous activity, reactivity, touch response, pain response, and gait), and autonomic (defecation and urination) profiles continuously for 24 h. Then animals were observed for 14 days for mortality (Parasuraman, 2011). The Wistar rats were divided into five groups comprising of 5 animals each. Group I was normal control while group II was diabetic control. The group III was diabetic rats treated with glibenclamide (0.25 mg kg^{-1}) orally for 28 days and group IV was diabetic rats treated with resistant starch (@ 100 mg kg^{-1}) orally for 28 days. The group V was diabetic rats treated with resistant starch @ 200 mg kg^{-1} orally for 28 days. Diabetes was induced in overnight fasted rats by administering single intraperitoneal injection of freshly prepared streptozotocin (STZ) 50 mg kg^{-1} body weight, followed by 120 mg kg^{-1} nicotinamide (NIC) in 0.1 M citrate buffer (pH 4.5) in a volume of 0.5 mL kg^{-1} body weight (Annadurai *et al.,* 2012). Diabetes was confirmed in STZ + NIC treated rats by measuring fasting blood glucose levels after 48 h of induction. After 24 h of STZ + NIC injection, the rats were given 5% w/v glucose solution (2 mL kg^{-1} body weight) to prevent hypoglycemic mortality. Rats with fasting blood glucose >180 mg dL^{-1} were considered diabetics and divided randomly into four groups. The standard glibenclamide and resistant starch were separately suspended in 1% w/v carboxymethyl cellulose and administered once daily through oral passage for 28 consecutive days.

The blood samples were collected on 1st, 14th, and 28th day of the treatment, through tail vein of rats by pricking and were immediately used for the estimation of blood glucose with a glucometer. Weekly body weight variations were monitored for all the experimental animals. At the end of experiment, the blood samples were withdrawn from all the experimental animals through retro-orbital plexus puncture in plain and sodium ethylenediamine-tetraacetic acid (EDTA) tubes for biochemical analysis (Lowry *et al.,* 1951). Finally, the animals were sacrificed by diethyl ether anaesthesia, and liver and pancreatic tissues were excised and used for biochemical and pathological

analysis. Part of the tissue sample was preserved in an ice-cold container for biochemical analysis and the remaining was stored in 10% formalin solution for histopathologic analysis.

Biochemical analysis

The whole blood sample was used for the estimation of glucose (One-Touch Horizon glucometer; ortho-clinical diagnostics, Johnson & Johnson Co.), hemoglobin, and glycosylated hemoglobin (HbA1c). The plasma sample was used for the estimation of insulin (Radioimmunoassay kit, Meridian Bioscience). The serum was used for the estimation of biochemical markers such as creatinine, urea, protein, liver glycogen, total serum cholesterol, serum triglyceride, high density lipoprotein (HDL) cholesterol (Parasuraman *et al.,* 2020). The biochemical markers were measured using a biochemistry analyser (Merk Misrolab 300, Elitech) and the LAB-KITS enzymatic kits (Meridian Bioscience) The liver tissue homogenate was used for the estimation of protein and glycogen. (Lowry *et al.,* 1951)

Histopathological study

A portion of pancreatic tissue was dissected out and fixed in 10% buffered neutral formal saline and processed. After fixation, tissues were embedded in paraffin. Fixed tissues were cut at 5 µm and stained with haematoxylin and eosin. The sections were examined under light microscope at 40 x magnification and photomicrographs were taken (Lowry *et al.,* 1951).

Statistical analysis

All the data were expressed as mean ± SEM. Statistical significance between the groups were tested using one-way analysis of variance (ANOVA) followed by Newmann Keul's multiple range tests. $P < 0.05$ was considered significant.

RESULTS AND DISCUSSION

Various plant species are a part of folk medicine in different cultures and are frequently used as a treatment option against DM across the world. Although different oral and systemic anti-diabetic agents are available in the market, the need for natural anti-diabetic products is increasing as a complementary remedy (Kooti *et al.,* 2016).

Acute toxicity of resistant starch derived from A. campanulatus

The resistant starch of *A. campanulatus* showed no toxic signs even 24 h after its administration. Further, no oral toxicity or mortality was detected after oral administration of higher doses (up to 2000 mg kg^{-1}) of resistant starch. This indicates the safety of resistant starch for prolonged use.

The resistant starch did not show any mortality or adverse effect up to the dose of 2000 mg kg^{-1}. Hence, the study was carried out at the dose levels of 100 and 200 mg kg^{-1}. The prebiotic growth promotion mechanism and relationship between prebiotic and probiotic have been extensively documented (Oliveira *et al.,*2011). The new dimension of prebiotics describes substance as non-carbohydrate and also the site of action is neither restricted to GI tract nor its type is limited to food. Different other prebiotics emerging from plant sources reported include polyphenols from blue berries, wine grape seed, and orange albedo, catechin, and punicalagin from fermented pomograntes, polypeptide polymers like poly-gamma glutamate (PGA) from fermenting *Bacillus* culture, algal polysaccharides, resistant starch from lotus seed, Longan pulp polysaccharides, etc. (Choudhury *et al*., 2017).

Effect of resistant starch on body weight

The rats treated with resistant starch from *A. campanulatus* showed significant increase in their body weight just like normal control rats (Table 1). In diabetic control group, severe body weight loss was noted, probably due to the increase in muscle wasting and tissue protein loss. In present study,

treatment groups showed significant improvement in body weight, revealing that resistant starch and glibenclamide prevent hyperglycemia-induced muscle wastage.

Effect of resistant starch on blood glucose, plasma insulin levels and other biochemical parameters

In present study, diabetic control rats showed severe hyperglycemia as compared to the normal rats. The mean blood glucose level in diabetic control group on day 0 and 28 was 275.3 ± 5.4 and 293.2 ± 6.5 mg dL^{-1}, respectively (Table 2). The standard drug glibenclamide lowered blood glucose level significantly, bringing it back to near normal level; whereas resistant starch from *A. campanulatus* @ 100 and 200 mg kg^{-1} significantly decreased the fasting blood serum glucose level in diabetic rats on 4th and 28th day as compared to the diabetic control group. The reduction in glucose levels may be due to the increase in plasma insulin levels or enhanced transport of blood glucose in peripheral tissue. From the study it is evident that resistant starch increased plasma insulin levels and showed promising antidiabetic activity. Diabetic animals showed enhanced levels of HbA1c due to excessive production of glucose in blood, which further reacted with blood hemoglobin and produced HbA1c. The reports indicate that the rats treated with nicotinamide/streptozotocin produce type 2 DM, but rats treated with streptozotocin alone induce type 1 DM (Ahangarpour *et al.*, 2016). Streptozotocin selectively damages insulin-secreting β-cells of pancreas, thereby produces a diabetic condition. The insufficient level of insulin further induces cell's disability to use glucose and subsequently produces reactive oxygen species (Yan and Wu, 2015). However, nicotinamide partially protects pancreatic β-cells against streptozotocin by inhibition of poly-adenosine diphosphate ribose-ribose polymer-ase-1 activity and serves as a precursor of nicotinamide adenine dinucleotide. The experimental rats showed various diabetic complications, such as cardiomyopathy, retinopathy, nephronpathy and neuropathy, which develop through oxidative stress induced mechanisms (Rani *et al.*, 2019). The prebiotics play a vital role in the control of DM due to its inherent capacity to modulate gut microbiota and improve the gastrointestinal tract implicating anti-diabetic efficiency. The pivotal role of RS in the reduction of blood glucose levels are well documented with clinical trials of oral administration with RS

Table 1: Effect of resistant starch derived from *A. campanulatus* on body weight in streptozotocin and nicotinamide STZ + NIC) induced type-2 diabetes in rats

Treatments	Body weight (g)		
	0 day	14 day	28 day
Normal control	205 ± 4.3	218 ± 5.8	240 ± 6.9
Diabetic control	212 ± 5.5	192 ± 4.7*[a]	175 ± 4.2*[a]
Standard control: Glibenclamide oral treatment @ 0.25 mg kg^{-1} for 28 days	218 ± 5.9	230 ± 6.2	248 ± 7.4
Resistant starch treatment @ 100 mg kg^{-1} orally for 28 days	220 ± 6.2	232 ± 6.4	246 ± 7.2
Resistant starch oral treatment @ 100 mg kg^{-1} for 28 days	210 ± 4.8	222 ± 5.9	237 ± 6.3

Values are expressed as mean ± SEM; *a Values are significantly different from normal control

Table 2: Effect of resistant starch, derived from *A. campanulatus*, on fasting blood glucose levels (mg dL^{-1}) in STZ and NIC induced diabetic rats

Treatments	Blood glucose (mg dL^{-1})		
	0 day	14 day	28 day
Normal control	95.8 ± 3.1	96.3 ±3.8	98.0 ± 4.4
Diabetic control	275.3 ± 5.4	284.8 ± 6.1*[a]	293.2 ± 6.5*[a]
Standard control: Glibenclamide oral treatment @ 0.25 mg kg^{-1} for 28 days	264.3 ± 5.1	155.9 ± 3.2*[b]	135.8 ± 3.1*[b]
Resistant starch treatment @ 100 mg kg^{-1} orally for 28 days	255.2 ± 4.6	165.4 ± 4.8*[b]	148.8 ± 3.9*[b]
Resistant starch oral treatment @ 100 mg kg^{-1} for 28 days	260.5 ± 5.3	172.3 ± 5.2*[b]	142.6 ± 3.4*[b]

Values are expressed as mean ± SEM; *a Values are significantly different from normal control; *b Values are significantly different from diabetic control

derived from inulin to the subjects with metabolic syndrome and improvement in insulin sensitivity revealing its therapeutic potential in type 2 DM treatment (Megur *et al.*, 2022). Besides, there is decrease in HbA1c and significant glucose control with prebiotic supplementation (Wang *et al.*, 2019).

The experimental evidences suggest that co-administration of hypoglycemic medicaments with prebiotic functional food supplement the management of type 2 DM (Robertson, 2020). The increased abundance of *Akkermancia muciniphila*, *Faecalibacterium prauznitzii*, *Bifidobacterium*, and *Roseburia* have been evidenced in intestinal microbiome of tested individuals co-administered with prebiotic based metformins (Vitetta *et al.*, 2023). The treatment modalities encompass the pharmacotherapy with adjuncts like prebiotic oligosaccharides in T2DM amelioration and relative correlation between gut microflora and diabetic control. The possibility of functional barrier mechanism in intestine by gut microbiomes against pathogenecity of DM were evidenced by the insulin resistance mechanism and glycaemic control evaluated in clinical trials. In these studies, the gut epithelium acted as barrier dysfunction by protecting the microflora and potential risk factors associated with inflammatory metabolites. Further, inulin degradative mechanism of probiotic *Bifidobacterium* by secretion of enzymes like β-fructanoside and β-galactoside indirectly corroborated to the decreasing blood glucose levels (Robertson, 2020).

Diabetic animals showed significant decrease in plasma insulin, hemoglobin, and HbA1c levels when compared with control animals. Resistant starch and glibenclamide reversed the insulin depletion in diabetic condition and brought hemoglobin and HbA1c back to the normal levels (Table 3). The resistant starch treated animals inhibited hyperglycemia induced by STZ + NIC which may be due to the free radical scavenging properties of the individual herbs present in it. The findings are in agreement with Jothilakshmi *et al.* (2016) who reported that blood glucose was significantly lowered in inulin extracted from Jerusalem artichoke (*Helianthus tuberosis*) administrated group from 204.16 to 121.16 mg dL^{-1} (a reduction of 40.65%) at the end of four weeks feeding trials.

Table 3: Effect of resistant starch, derived from *A. campanulatus*, on plasma insulin, glycosylated haemoglobin and haemoglobin levels in STZ + NIC induced diabetic rats

Treatments	Plasma insulin (μIU mL^{-1}) 28^{th} day	HB (mg dL^{-1})	HBA1c (%)
Normal control	18.60 ± 0.98	14.4 ± 0.88	6.15 ± 0.45
Diabetic control	6.45 ± 0.47*[a]	8.1 ± 0.72*[a]	12.88 ± 0.89*[a]
Standard control: Glibenclamide oral treatment @ 0.25 mg kg^{-1} for 28 days	17.30 ± 0.82*[b]	13.3 ± 0.82*[b]	7.05 ± 0.65*[b]
Resistant starch treatment @ 100 mg kg^{-1} orally for 28 days	14.7 ± 0.72*[b]	12.5 ± 0.78*[b]	7.80 ± 0.73*[b]
Resistant starch oral treatment @ 100 mg kg^{-1} for 28 days	15.8 ± 0.84*[b]	12.9 ± 0.80*[b]	7.40 ± 0.67*[b]

Values are expressed as mean ± SEM; *a = Values are significantly different from normal control; *b Values are significantly different from diabetic control

The resistant starch from *A. campanulatus* affected serum lipid profiles, except HDL as compared to the control group, whereas the levels in treatment group remained within normal range at the end of the study (Table 4). Diabetic rats showed significant reduction in liver glycogen and total protein as compared to the control group, whereas resistant starch and glibenclamide treated rats showed normal liver glycogen and total protein. The prevention of glycogen depletion in liver tissue was perhaps due to the stimulation of insulin release from β cells that activates glycogen synthase system.

In renal dysfunction, that is induced by diabetic hyperglycemia, the serum urea and creatinine levels are markedly elevated. In present study, diabetic rats showed elevated serum creatinine and urea suggesting impairment of kidney in filtering the toxic or waste products out of the body. Further, serum creatinine and urea levels were considerably diminished in resistant starch treated diabetic rats, suggesting a renoprotective effect on diabetic rats. STZ + NIC diabetic rat has increased levels of lipid peroxides and reactive oxygen species, which cause hyperglycemia. Incessant generation of free

radicals can lead to tissue damage through peroxidation of unsaturated fatty acids (Kumar *et al.*, 2014).

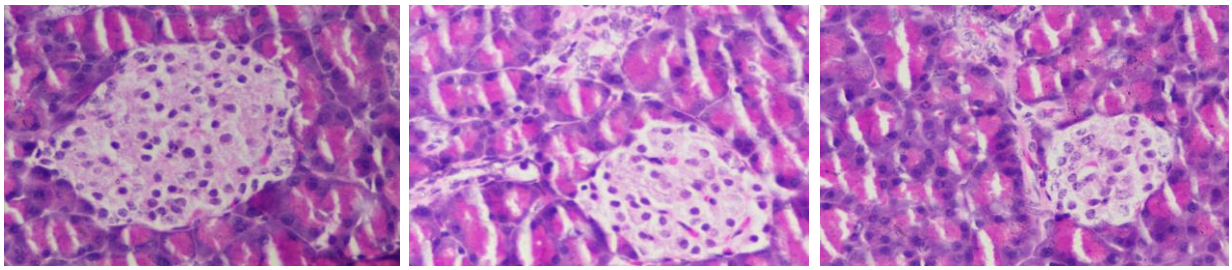
Histopathology

The histopathologic studies of pancreas revealed severe congestion, huge decrease in the number of islets of Langerhans and β cells, and fibrosis and inflammatory cell infiltration into the islets of Langerhans in STZ and NIC induced hyperglycemic rats (Fig. 1). These observations were made by using 40 x frame microscopic magnification. The resistant starch from preparation of *A. campanulatus*

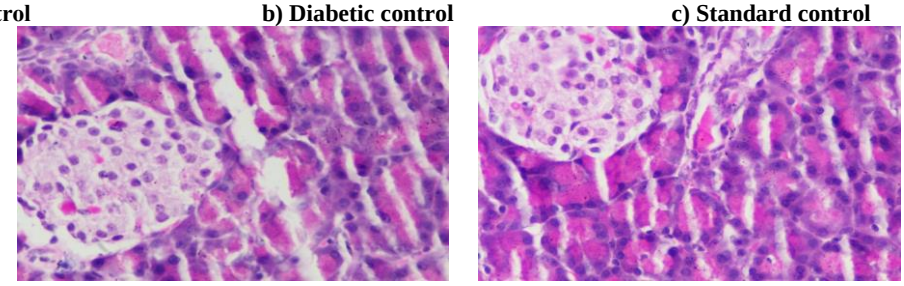
Table 4: Effect of resistant starch, derived from *A. campanulatus*, on different biochemical parameters in streptozotocin (STZ) and nicotinamide (NIC) induced type-2 diabetes in rats

Treatments	Liver glycogen (mg 100 g^{-1} wet tissue)	Total protein (mg dL^{-1})	Urea (mg dL^{-1})	Creatinine (mg dL^{-1})	Trigly-ceride (mg dL^{-1})	Total cholesterol (mg dL^{-1})	HDL (mg dL^{-1})
Normal control	5.58 ± 0.60	9.53 ± 0.77	33.5 ± 1.30	1.08 ± 0.12	145 ± 3.22	82.3 ± 1.45	44.2 ± 1.70
Diabetic control	2.18 ± 0.12*a	4.20 ± 0.38*a	81.80 ± 2.45*a	3.20 ± 0.38*a	260 ± 5.75*a	175.7 ± 3.85*a	25.3 ± 0.95*a
Standard control: Glibenclamide oral treatment @ 0.25 mg kg^{-1} for 28 days	5.47 ± 0.52*b	9.08 ± 0.65*b	40.3 ± 1.43*b	1.22 ± 0.18*b	168 ± 4.50*b	91.2 ± 1.50*b	39.4 ± 1.58*b
Resistant starch treatment @ 100 mg kg^{-1} orally for 28 days	5.02 ± 0.38*b	8.18 ± 0.55*b	47.2 ± 1.58*b	1.34 ± 0.30*b	180 ± 4.70*b	98.4 ± 2.35*b	32.25 ± 1.40*b
Resistant starch oral treatment @ 100 mg kg^{-1} for 28 days	5.29 ± 0.42*b	8.55 ± 0.60*b	43.8 ± 1.49*b	1.30 ± 0.23*b	173 ± 4.65*b	94.8 ± 2.22*b	36.7 ± 1.47*b

Values are expressed as mean ± SEM; *a: Values are significantly different from normal control; *b: Values are significantly different from diabetic control



a) normal control **b) Diabetic control** **c) Standard control**



d) Resistant starch treatment @ 100 mg kg^{-1} **e) Resistant starch treatment @ 200 mg kg^{-1}**

Fig. 1: Histopathological micrographs showing a) healthy Langerhans and β cells in normal animal body; b) diabetic cells showing severe congestion, huge decrease in the number of Islets of Langerhans and β cells, and fibrosis and inflammatory cell infiltration into Islets of Langerhans in STZ + NIC induced hyperglycemic rats; c) Standard control: Glibenclamide oral treatment @ 0.25 mg kg^{-1} for 28 days, cells showing moderate congestion with moderate decease in the number of Islets of Langerhans and β cells, and mild lymphocytic infiltration; d) & e) Resistant starch (from *A. companulatus*) treatment @ 100 and 200 mg kg^{-1}, respectively, showing mild congestion and mild decrease in the number of Islets of Langerhans with normal β cell population, indicating significant recovery (microscopic magnification 40X)

@ 100 and 200 mg kg^{-1} showed mild congestion and mild decrease in the number of islets of Langerhans with normal β cell population, indicating significant recovery. Glibenclamide treatment showed moderate congestion with moderate decrease in the number of islets of Langerhans and β cells and mild lymphocytic infiltration. The photomicrograph of diabetic pancreatic tissue clearly showed the streptozotocin + nicotinamide induced damage in both exocrine and endocrine components of pancreatic tissue. Glibenclamide stimulates the pancreatic islets regeneration and is responsible for the increase in plasma insulin as observed during biochemical evaluations and the histological photomicrograph (Oche *et al.*, 2014). It was observed that the flour mix preparation of *Amorphophalus campanulatus* showed protective activity against ROS-mediated damage, which occurs in the islets of Langerhans cells of pancreas.

Conclusion: The study demonstrates the antidiabetic potential of resistant starch from *Amorphophallus campanulatus* @ 100 and 200 mg kg^{-1}. The treatment effectively reduced blood glucose, HbA1c, cholesterol, and renal biomarkers, while increasing plasma insulin, HDL cholesterol, liver glycogen, and total protein levels. These effects were comparable to glibenclamide, highlighting the therapeutic promise of *A. campanulatus* resistant starch in diabetes management. Future research should explore its clinical efficacy and study the underlying mechanisms. The findings suggest that incorporating resistant starch into diabetes care could offer a natural adjunct to conventional treatments.

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Conflicts of interest: The authors declare no conflict of interest.

Ethical statement: The study was executed after the approval from the Institutional Animal Ethical Committee of K.M. College of Pharmacy vide No. IAEC/Dr. K. Jothilakshmi /TNAU/UP17GPT9770007/KMCP/18/2023-24.

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