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Antidiabetic activity of actinidia deliciosa fruit in alloxan induced diabetic rats

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Abstract
Background: The aim of the present study is to evaluate antidiabetic activity of methanolic extract of Actinidia deliciosa fruit in alloxan induced albino Wister rats.
Methods: Actinidia deliciosa fruit extract or metformin was administered to the rats orally for seven days. Levels of Blood Glucose, Triglycerides, Cholesterol, HDL cholesterol, SGOT and SGPT were used to evaluate its antidiabetic effects in Albino Wister rats.
Results: Blood glucose, Triglycerides, Cholesterol, HDL cholesterol, SGOT and SGPT levels were significantly increased in alloxan induced diabetic rats to compare to the normal group. After seven days treatment with Actinidia deliciosa extract showed the significant decrease in the diabetic control group and metformin also showed a significant decrease in diabetes.
Conclusion: Our results suggest that the methanolic extract of Actinidia deliciosa fruit clearly demonstrated the antidiabetic activity in an experimental model of rats.

Keywords: Actinidia deliciosa, type-2 diabetes, metformin, alloxan, albino wister rats

1. Introduction
Diabetes Mellitus is the most devastating human endocrine disease and pancreatic islet disorder with multiple aetiology [1, 2]. It is considered to be a heterogenous metabolic disorder [3] characterised by hyperglycaemia resulting from a variable interaction of hereditary and environmental factors [4]. Due to absolute or relative deficiency or diminished effectiveness of circulating insulin [5].Diabetes mellitus is associated with chronic complications like microvascular, macrovascular disorders [6]. Such as renal failure, coronary artery disorder, cerebrovascular disease, neurological complications, blindness, limb amputation, long term damage dysfunctions failure of various organs [7]. Other factors such as dyslipidemia or hyperlipidemia are also involved in the development of micro and macrovascular complications of diabetes, and these are major causes of morbidity and mortality [8]. According to present criteria, India has been considered, the diabetic capital of the world. More than 50.8 million are affected with diabetes in India, and this may rise to 87 million by the year 2030 [9]. Globally, an epidemic of diabetes mellitus is a problem of public health with greater or worse condition in developing countries than the developed countries [1].Where adequate treatment is often expensive or unavailable [10]. Type 2 diabetes mellitus is associated with increased glucose production, Diminished insulin secretion, and impaired insulin action [11]. Glucolipotoxicity is the two contributing factors for the β – cell dysfunction in type 2 diabetes mellitus [12]. Various risk factors which show influence in the development of type 2 diabetes mellitus are carbohydrate enriched food supplement, stress, sedentary life style, smoking and alcohol consumption.
Therapeutics agents like insulin, sulfonylureas, biguanides and thiazolidinedione derivatives and α glucosidase inhibitors are preferred [2]. To reduce the hyperglycemic condition. The drugs that are preferred for treatment such as **s**ulfonylureas which stimulates pancreatic islets to secrete insulin. Biguanides which are responsible for the reduction of hepatic glucose output. Thiazolidinedione derivatives exert their peripheral action by lowering insulin resistance in peripheral tissue. α – glucosidase inhibitors augment glucose utilisation and responsible for suppression of glucose production [13, 14]. Apart from the therapeutic option for diabetes like oral hypoglycemic and insulin have some adverse effects [15]. Hence the current therapy is focused on herbal medicines [16]. And they are used for current therapy due to presumed effectiveness, relatively low cost, presumed fewer side effects and low toxicity [5].
The medicinal plants might provide a useful source of new oral hypoglycemic compounds, and this may lead to the development of pharmaceutical entities, and this may act as a dietary

adjunct to existing therapies [17]. Worldwide there are more than 1200 plant species, some of the medicinal plants that are used to control blood glucose levels such as Azadirachta Indica, Catharanthus roseus, Allium Sativum, Memordica judaica, Aloe Vera, Trigonella foenum graecum [18, 19]. Due to the presence of active principles in medicinal plants they have been reported to possess some characteristic properties like pancreatic β cell regenerating, insulin-releasing and fighting the problem of insulin resistance [20].

Among them one such plant is Actinidia deliciosa, it is commonly known as kiwi fruit, and the species is native to China. It belongs to Actinidiaceae family [21]. The root of Actinidia deliciosa is considered as one of the traditional drug in China [22]. Dietary fibre, Protein, Calcium, Iron, various Vitamins like Thiamine (Vitamin B1), Riboflavin (Vitamin B2), Niacin (Vitamin B3), Vitamin B6, Folate (Vitamin B9), Vitamin E, Vitamin K are considered to be the good sources of Actinidia deliciosa.

Based on some reports, roots of Actinidia deliciosa act as a folk remedy for adult diseases such as antihepatotoxic, anti-pyorrheal and gingival inflammation, and showed to have antitumor and protective effects on acute hepatic injury in biological arrays [23]. To know the blood sugar lowering properties of Actinidia deliciosa in type 2 diabetes, we therefore aimed to evaluate the antihyperglycemic effect of Actinidia deliciosa in alloxan induced diabetic rats.

2. Materials and methods

2.1Chemicals

Alloxan and metformin were purchased from Sigma Aldrich, Mumbai, India.

2.2 Collection of plant

The fruits of Actinidia deliciosa were procured, and its authentication was done by prof. Dr.Ajmeera Ragan, Department of Botany, Kakatiya University, Warangal (Dist.), Andhra Pradesh (State), India.

2.3Preparation of plant extract

Fruit pieces were sun dried and undergone for maceration process. In this process, the coarsely powdered crude drug is placed in a stoppered container with the solvent (Methanol) and allowed to stand at room temperature for at least three days with frequent agitation until the soluble matter has dissolved. The mixture is then strained, the Marc (the damp solid material) is pressed, and the combined liquids are clarified by filtration or decantation after standing.

2.4 Experimental Animals

Experiments were performed on Albino Wister male rats (150 -200g). Animals were procured from the animal house and maintained on a natural day – night cycle (12hr dark: 12hr light) at room temperature of about 24-26 ^{O} C. with free access to standard food pellets and water ad libitum. The experimental protocol was approved by the Institutional Animal Ethics Committee.

2.5Induction of diabetes

A single dose of Alloxan was dissolved in sterile normal saline immediately before use and injected intraperitoneally at a dose of 120mg/kg. Diabetes developed gradually and was assessed after three days. Rats are having blood glucose levels greater than 250mg/dl indicates induction of diabetes mellitus (Prashant Chaudhary *et al.* 2012).

2.6 Experimental design

In the experiment, a total of 30 rats were used. The rats were divided into five groups of six each. Group 1 served as control; Group 2 were diabetic rats; Group 3 were diabetic rats given Actinidia deliciosa fruit extract 500 mg/kg, p.o; in 1ml of aqueous solution for 7 days; Group 4 were diabetic rats given Actinidia deliciosa fruit extract 1000mg/kg, p.o; in 1ml of aqueous solution for 7 days; Group 5 were diabetic rats given metformin (10mg/kg), p.o; in 1ml of aqueous solution for 7 days.

2.7Blood collection

After seven days of the treatment, blood samples were collected by puncturing the retro-orbital plexus (under light ether anaesthesia) using capillary tubes in fresh vials and centrifuged. The serum was immediately used for various biochemical estimations.

2.8 Biochemical assays

Blood glucose level, TG, Cholesterol, HDL cholesterol, SGPT and SGOT were estimated using commercial diagnostic kits (M/S Excel Diagnostics Pvt. Ltd. Hyderabad, India)

2.9 Histopathological studies

Histology of pancreas was studied using hematoxylin and eosin (H and E) and oil red O Staining. Thin sections (4-5 m) were cut and stained with H and E. For oil red O staining, frozen pancreas sample was processed using cryostat and then fixed and stained.

2.10 Statistical analysis

All biochemical results were expressed as mean ± SEM. Significant differences among the groups were determined by one-way Analysis of Variance (ANOVA) followed by Dunnett test. Statistical significance was considered at $P < 0.05$.

3. Results

3.1 Effect of Actinidia deliciosa fruit extract on body weight in alloxan- induced diabetic rats: On seven days treatment, there was no significant change in body weight in alloxan induced diabetic rats compared to normal rats.

3.2 Effect of Actinidia deliciosa fruit extract on blood glucose level in alloxan- induced diabetic rats:

Blood glucose levels were significantly increased in alloxan induced diabetic rats to compare to the normal group. After 7days treatment with Actinidia deliciosa extract (500mg/kg, 1000 mg/kg) had shown the significant decrease in the diabetic control group and metformin also showed a significant decrease in diabetes.

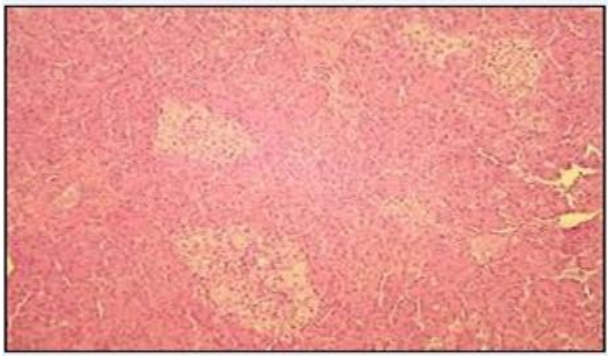
3.3 Effect of Actinidia deliciosa fruit extract on TG, TC & HDL in alloxan- induced diabetic rats: TG, TC and HDL were significantly increased in alloxan induced diabetic groups compared to the normal group. Treatment with Actinidia deliciosa extract (500mg/kg, 1000mg/kg) and metformin once daily for seven days, showed the significant decrease in diabetic control.

3.4 Effect of Actinidia deliciosa fruit extract on SGOT & SGPT in alloxan- induced diabetic rats: SGOT& SGPT levels were significantly increased in alloxan induced diabetic groups compared to the normal group. Treatment with Actinidia deliciosa extract (500mg/kg,1000 mg/kg) and metformin once daily for seven days, showed the significant decrease in diabetic control.

Table 1: Effect of Actinidia deliciosa fruit extract on

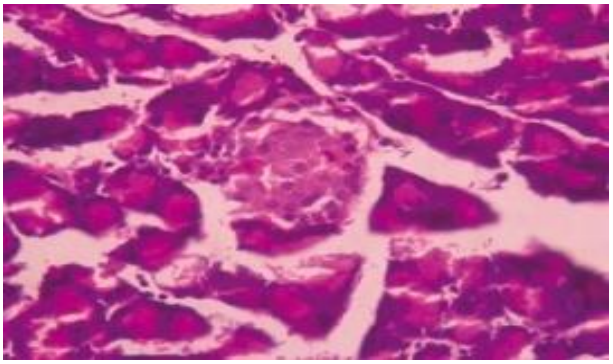
Groups	Blood glucose	Triglycerides	Cholesterol	HDL	SGOT	SGPT
Normal control	119.7±1.33	92.8± 1.53	107.7± 1.54	41.8±0.94	92.17± 1.07	86±1.29
Diabetic control	269±1.16 **	168.8± 1.97 **	223.5±2.44 **	23.6±1.62	129.5± 1.74 **	120.7±1.16 **
A.D low dose (500mg/kg)	186±1.75 **	149.2± 1.352 **	169± 1.65 **	33.5±1.56 **	113.5± 1.87**	111.2± 0.94 **
A.D high dose (1000mg/kg)	151.2±1.12**	125.2± 1.70**	139± 1.88 **	38.6 ±0.98 **	103.7± 1.25**	101± 1.29 **
Metformin	121.3±1.25**	94.6±1.43**	109.7± 1.88 **	44±0.89 **	94± 1.18**	88.3± 0.88 **
*P< 0.05 Significant, **P< 0.001 highly significant						

Pancreatic section of normal rat showed the normal morphology of beta cells. In diabetic control rats, the pancreas section was shown with damaged islets in an irregular form. Treatment with Actinidia deliciosa extract (500mg/kg, 1000mg/kg) and standard drug metformin, respectively showed improvement in beta cell structure.



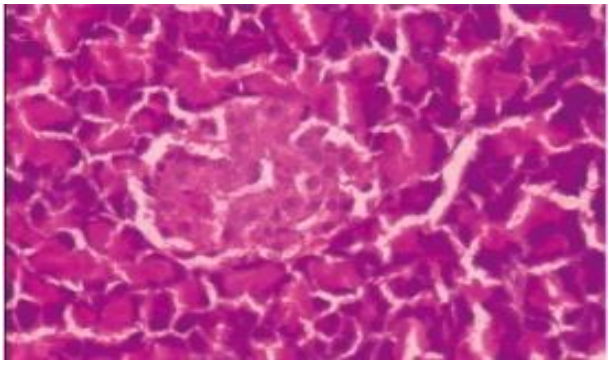
(a)Histopathology of normal group

Normal rats show normal islets

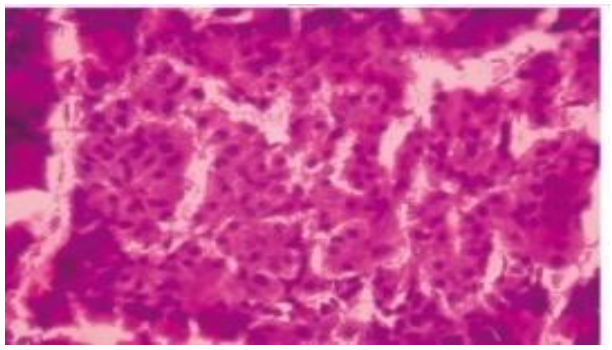


(b)Histopathology of diabetes induced by alloxan group

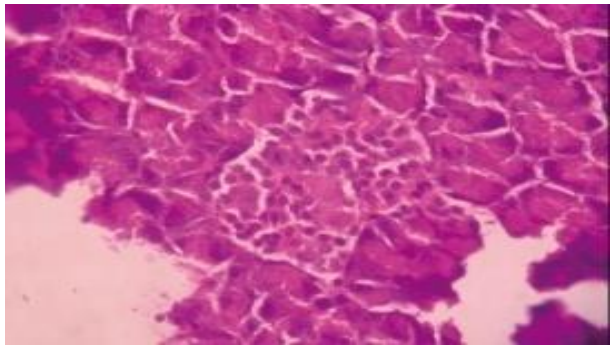
Alloxan (120mg/kg) induced diabetic rats to show abnormal



(c) Histopathology of Actinidia deliciosa 500mg/kgb.w. treated group
The Structure of pancreas is partially the islets are normal



(d) Histopathology of Actinidia deliciosa 1000 mg/kg b.w.treated group



(e)Histopathology of Standard drug (Metformin)

Metformin (10mg/kg) treated rats islets shows depletion of cells

Fig (a-e): Histopathology of pancreas in alloxan induced diabetic rats

4. Discussion

The management of diabetes with the agents devoid of any side effects is still a challenge to the medical system. This concern has led to an increased demand for natural products and the treatment of diabetes with medicines of plant origin that proved much safer than synthetic drugs [2, 16]. Literature shows that the alloxan monohydrate is one of the chemical agents, and it is used for the induction of diabetes mellitus [14]. Alloxan is responsible for pancreatic islet β- cell cytotoxicity. The cytotoxic action of alloxan is mediated by reactive oxygen species with a simultaneous massive increase in cytosolic calcium concentration, leading to a rapid destruction of beta cells [2]. In our study, the significant increase in blood glucose was observed in alloxan induced diabetic rats and when diabetic rats administered orally with methanolic extract of Actinidia deliciosa fruit (500mg/kg & 1000mg/kg) and standard drug metformin, a reduction in glucose levels were observed. Hence proven that the Actinidia deliciosa extract may act by stimulating utilisation of glucose by peripheral tissue or the involvement of hepatic factors like activation of

glycogen synthetase, which was supported by the literature [7]. According to experimental study, a marked increase in the level of cholesterol and triglycerides were observed in untreated diabetic rats. The diabetic treated rats showed a reduction in the level of cholesterol and triglycerides. When compared with untreated diabetic rats and this shows the beneficial effect of plant extract [4]. The present study revealed that the increased level of SGOT and SGPT were observed in the diabetic-induced rats. In Actinidia deliciosa treated and metformin-treated rats the level of SGOT and SGPT were restored to a normal level [7]. The high-density lipoprotein (HDL) was significantly reduced in diabetic rats, and increased levels were seen in plant extract treated animals, which was agreed with the report of [19]. Quercetin which is a principle constituent of Actinidia deliciosa shows the hypoglycemic effect in experimental rats. This is in support of present finding which showed that the extract of Actinidia deliciosa was found to be effective against alloxan-induced diabetic rats [5]. The histological studies of the endocrine region of the pancreas of the diabetic and Actinidia deliciosa fruit extract treated animals revealed that shrinkage of β – cells of islets of langerhans in diabetic animals. The restorations of the β- cells in diabetic treated animals corroborate the increased serum insulin levels in treated animals. Statistical analyses of observations suggest that the methanolic extract of Actinidia deliciosa have potential anti- hyperglycemic properties.

5. Conclusion

In conclusion, the methanolic extract of Actinidia deliciosa fruit at the doses of 500mg/kg and 1000mg/kg clearly demonstrated antidiabetic activity in an experimental model of rats.

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