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Research Article

EVALUATION OF ANTI-DIABETIC ACTIVITY OF METHANOLIC EXTRACT FROM THE FRUIT PEEL OF *ATALANTIA MONOPHYLLA* (*LINN.*) IN ALLOXAN INDUCED DIABETIC MICE

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ABSTRACT

Objective: *Atlantia monophylla* is an indigenous medicinal plant, with a folk reputation as hypoglycemic agent throughout India. Considerable research has shown that plants rich in flavonoids content with anti-oxidant potential are known to be bioactive for the management of diabetes mellitus (DM). In the present investigation, hypoglycemic activity of aqueous fruit peel extract of *A. monophylla* was evaluated using alloxan-induced hyperglycemic mice.

Methods: Aqueous extract of the fruit peel of *A. monophylla* (AEAM) was subjected to preliminary phytochemical screening and acute oral toxicity study as per Organization for Economic Cooperation and Development guidelines 425. AEAM was evaluated for hypoglycemic activity, Alloxan induced DM in mice, oral glucose tolerance test in fasted mice. *In vitro* α- amylase inhibitory in albino mice method was employed for evaluation of hypoglycemic activity.

Results: All of the mice in each group had their blood glucose levels measured both before and after the treatments on fasting animals. The extract was given at doses of 200 mg/kg and 400 mg/kg body weight, or 100 mg/kg body weight of the conventional antidiabetic medication Metformin. A glucometer was used to measure the blood glucose level. After 1 h, 2 h, and 4 h, the extract-treated diabetic mice had a substantial ($p \leq 0.05$) drop in blood glucose levels. The hypoglycemic action was similar to that of the medication Metformin used as a benchmark.

Conclusion: The results of this study indicate that AEAM has strong hypoglycemic properties. One such method might include the activation of insulin receptors and subsequent release of insulin once β cells are stimulated. The hypoglycemic effect of the plant could be achieved through increasing insulin release from the pancreas.

Keywords: Diabetes mellitus, *Atlantia monophylla*, Hypoglycemic, Metformin.

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INTRODUCTION

Diabetes is characterized by weight loss and polyuria, and it was initially recorded by the Egyptians. However, the term diabetes mellitus (DM) was first used by the Greek physician Aertaeus. Diabetes means "to pass through" in Greek, while the Latin term mellitus means "honey" (relating to sweetness) [1].

It is a combination of heterogeneous disorders commonly presenting with episodes of hyperglycemia and glucose intolerance, as a result of lack of insulin, defective insulin action, or both [2]. Many pathogenic processes are involved in the diabetes development. These include autoimmune destruction of pancreatic b-cells and the resulting insulin shortage, as well as other abnormalities that lead to resistance to the action of insulin [3]. Diabetes-related anomalies in the metabolism of fat, protein, and carbohydrates are caused by insufficient insulin action on target tissues. It decreased tissue responses to insulin and/or insufficient insulin production at one or more stages in the intricate pathways of hormone action and results into deficient insulin action. The major challenges to control hypoglycemia and associated symptoms are optimally managing the patient with DM and are targeted at reducing complications, and improving life expectancy and quality of life. Valuable information from research and development applies directly to improving outcomes in patients with DM [4].

Type II diabetes is the most predominant form of diabetes and accounts for at least 90% of all cases of DM [5]. The rise is predicted to be much greater in developing than in developed countries [6]. In developing countries, people aged 40–60 years (that is, working age) are affected most, compared with those older than 60 years [2]. This increase in Type II diabetes is linked to changes toward a Western lifestyle (high diet with minimal physical activity) in developing countries and the rise in obesity [7,8]. There are approximately 1.4 million people who have diagnosed with Type II diabetes in the United Kingdom [9]. The incidence of diabetes enhances along with age, most of the cases being diagnosed after the age of 40 years. This equates to a lifelong risk of developing diabetes of 1 in 10 [10].

The herbal medicines industry has grown exponentially in recent years. Due to their natural origin and their minimal side effects, these medicines are gaining great popularity in both developed and developing countries. Medicinal plants, minerals, and organic matter are the sources of many common traditional medicines that are used [11]. Many medicinal herbs known as Rasayana, which have been utilized for over a millennium, are included in herbal remedies used in Indian traditional medical systems [12]. The majority of medical professionals in Indian systems create and administer their own concoctions. 21,000 plants are classified by the World Health Organization as being used medicinally worldwide. Of these 2500 species, 150 are employed on a reasonably considerable scale in commercial settings in India. In case of medicinal herbs, India is the largest producer and is called as botanical garden of the world [13].

Recently, there have been reports from all over the world that some medicinal plants can help with diabetes. These plants have been experimentally utilized as antihyperlipidemic and antidiabetic

treatments. Despite the presence of known antidiabetic medicine in the pharmaceutical market, diabetes and the related complications continue to be a major medical problem. The capacity of these plants to facilitate metabolites in insulin-dependent activities, limit intestinal glucose absorption, or restore pancreatic tissue function is thought to be responsible for their antihyperglycemic actions [14]. There are about 400 plant species with hypoglycemic action that have been documented in the literature; yet, the quest for novel natural plant-based antidiabetic medications remains compelling due to the presence of compounds that exhibit safe and alternative effects on DM. Glycosides, alkaloids, terpenoids, flavonoids, cartenoids, etc., found in the majority of plants, are commonly linked to antidiabetic effects. Medicinal herbs as potential source of therapeutics aids have attained a significant role in health system all over the world for both humans and animals not only in the diseased condition but also as potential material for maintaining proper health. Many synthetic medications have been linked to adverse consequences and even fatalities in humans; however, a plethora of herbal remedies are accessible to cure DM and prevent these unwanted effects. Herbal drugs do not show any side effects and are less expensive as compare to synthetic drugs. *Atlantia monophylla* commonly named as wild lemon or makad limbu, belongs to family Rutaceae is being used for treatment for various diseases conditions such as anti-inflammatory, ovicidal activity, mosquitocidal activity, antiparalytic, and as immunomodulation. Early study has shown that the plant possesses antidiabetic activity of *A. monophylla* bark, therefore present study seeks to determine whether *A. monophylla* fruit peels shows hypoglycemic effect in *in-vitro* and *in-vivo* models [15].

METHODS

Preliminary photochemical screening

Pharmacological screening

Experimental animals

Swiss albino mice of both sex weighing approx. 25–30 g was procured from National Institute of Biosciences, Dhangawadi, Nigadewada road, off Pune Bangalore highway, Tal. Bhor, dist.: Pune, pin code: 412205. The animals were kept in a 12:12 light/dark cycle, air-conditioned environment with a temperature of 23–25°C and a humidity level of 45–55%. Water was available to the animals at all times, along with normal laboratory rodent food (produced by Pranav Agro Industries Ltd., Sangli, India).

The animals were acclimatized to the laboratory conditions before commencement of the experiment. The Institute for Laboratory Animal Research (1996) and the Organization for Economic Cooperation and Development (OECD) (2008) stipulated that all research involving animals must comply with international guidelines, and the Committee for Control and Supervision on Experimental Animals (CPCSEA) governed the establishment of the Institutional Animal Ethics Committee (IAEC), which authorized all animal tests.

Chemicals

Alloxan monohydrate was purchased from Sigma-aldrich, (St. louis, USA), Saline solution (0.9%w/v NaCl) was purchased from Ain Medicare, Maleate buffer (0.2M solution of acid sodium maleate, 8 g of NaOH, 23.02 g of maleic acid, 19.6 g of maleic anhydride), Phosphate buffer (0.15M, pH 7.4), picric acid, ether, sucrose solution, alpha-amylase, potato starch were utilized in an experimental procedure were purchased from Research lab (Mumbai). Metformin was obtained from, Cipla Pharmaceutical Pvt. Ltd., Indore. Analytical grade solvents and other compounds were all utilized.

Collection, identification and authentication of plant material

The fruits of *A. monophylla* were collected from Bhilar and Danavali villages situated in dist. Satara, during august 2016. Yashwantrao Chavan (YC) Institute of Science's herbarium received a plant specimen. It was identified and authenticated by Prof. J. Gayakwad, department of Botany, YC Institute of science, (No. BSI/WRC/Tech/2013/1094). At Shivaji University, Kolhapur's YC Institute of Science, a voucher specimen of the plant was placed for future use. Fruit was washed gently by rinsing on running water to remove dust particles and peels of fruit were removed and air-dried under shade. Dried fruit peels were then ground to a coarse powder using electric grinder. The powdered plant material was stored in air tight container.

Preparation of aqueous extract of *A. monophylla* fruit peels

Ultrasonication technique was used for extraction. Fruit peels of *A. monophylla* were shade dried and powdered with electric grinder. 10 gm powdered fruit peels of *A. monophylla* was taken in beaker and 50 ml of distilled water was added in each of beaker. The beakers were kept in sonicator for sonication extraction at different time intervals 15, 30, 45, and 60 min, respectively. The extract was filtered and collected in different petri plates. The petri plates were kept aside for evaporation at room temperature and collected extract was stored in refrigerator.

Preparation of drug solution

Accurately weighed quantity of Metformin was dispersed in normal saline solution (0.9%w/v). All the powdered fractions of the aqueous extract were accurately weighed, and then dispersed in normal saline solution. The appropriate stock solution of the drugs was prepared. The doses were administered orally by selecting the appropriate concentration of the stock solution. Normal saline solutions were used as control. Dosage forms of aqueous extracts and drug solutions were prepared freshly on the day of dosing and stored in airtight container.

Approval of research protocol

The CPCSEA, India's regulations and guidelines guided the establishment of the IAEC, which granted approval for the experimental procedure. (Protocol approval number was YSPM/YTC/PHARMA/06/2017.

Acute oral toxicity study

Healthy female Swiss albino mice of 25–30 g were used in acute toxicity studies as per OECD guidelines-425. After an overnight fast, the animals were split up into three groups, each consisting of five mice. Extracts Aqueous extract of the fruit peel of *A. monophylla* (AEAM) were administered at dose of 200 mg/kg, p.o. body weight. The mice were observed continuously for behavioral and autonomic profiles for 2 h and for any signs of toxicity or mortality up to 48 h (OECD-425, 2001).

Oral glucose tolerance test

Weigh the mice. Fast mice for 5 h. And prepare an experiment record sheet, sticks for glucose measurement and syringe for oral gavage of the Dextrose solution. Calculate and record the volume of 20% Dextrose solution required for each individual mouse for gavage as follows: Inject 2 g of dextrose/kg body mass. Cut the tip of the tail using clean surgical scissors. A small drop of blood placed on the test strip of the blood glucose meter. This is the baseline glucose level (t = 0) and is recorded in the experiment record sheet. Take 6 µL of whole blood in a tube for measurement of insulin. Spin the blood for 1min at 1300 rpm and collect the plasma). Store the plasma on ice in a clean tube. Orally gavage the mouse with the appropriate volume of glucose solution, as previously determined and start the timer. The blood glucose levels are measured at 0, 30, 60, 90, and 120 min after collection of plasma for once at 10, 30, 60µL glucose gavage. Samples for insulin determination (20 and 120 min for each sample), start the bleeding again by removing the clot from the first incision; massage the tail if blood flow is inadequate. Place a small drop of blood on a new test strip. Results are recorded in the record sheet. Ensure that further blood loss from the incision is minimal by briefly applying pressure to the incision after each measurement. Serum was separated and the glucose concentration was estimated using glucometer [16].

Alloxan-induced DM

Alloxan that had been recently dissolved in citrate buffer was injected intraperitoneally once to cause diabetes. (50 mM/L, pH 3) at a dose of 200 mg/kg body weight. The mice were subjected to sensitivity by application of xylene solution on the inside of both ears under anesthesia. Main experiment was started on day of diabetes induction [17].

Experimental design
Swiss albino mice of either sex weighing approx. 25 g were selected on random basis. Specific marking was done on paw region of each mouse with the picric acid for identification. Mice were fasted for about 3 h; provided free access to drinking water. These mice were then divided into two groups (n=3) as standard and control. Standard and control group composed of six mice in each while; test group had again two groups of six mice for two different dose levels. Group 1: Control group-Saline solution, 2 mL/kg, p.o., Group 2: Standard group-Metformin 100 mg/kg, p.o., Group 3: Test 1 group-AEAM 200 mg/kg, p.o., Group 4: Test 2 group-AEAM 400 mg/kg, p.o. [18].

Blood collection
The blood samples (500–750 µL) were collected tail vein plexus puncture of anaesthetized mice. Blood samples were collected at the time of grouping of animals (basal reading) and at 1st, 7th, and 14th day of treatment. Serum was isolated for biochemical assessment after blood was spun for 20 min at 3500 rpm. Evaluation of serum glucose level of all treatment groups and histopathological analysis of pancreases of treated as well as untreated groups of animals was carried out.

Estimation of various biochemical and tissue parameter
Hypoglycemic activity by *in vitro*α-amylase inhibitory activity method [19].

The α-amylase inhibitory activity of the fruit peels from *A. monophylla* (AEAM) was investigated for its potential to cause hypoglycemia *in vitro*. Four different concentrations of plant extract were prepared by dissolving in double distilled water. These were 2.5 mg/mL, 5.0 mg/mL, 7.5 mg/mL, and 10 mg/mL. A total of 20 µL of plant extract and 20 µL of 0.02M sodium phosphate buffer (pH 6.9 with 0.006M sodium chloride) containing α-amylase solution (0.5 mg/mL) were incubated for 10 min at 25°C. Each tube was filled with 20 µL of 1% starch solution in 0.02M sodium phosphate buffer (pH 6.9 with 0.006 M sodium chloride) every 5 s following the pre-incubation period. Incubation of this reaction mixture was then carried out for 10 min at 25°C. To halt the process, 1 mL of DNSA color reagent was added. After that, these test tubes were allowed to cool to ambient temperature for 5 min while being incubated in a bath of boiling water. At 540 nm, absorbance was measured after this reaction mixture had been diluted once again with the addition of 10 mL of distilled water. Calculate the percentage of inhibition by assuming the inhibition of α-amylase produced by the control group as 100% by following equation;

$$\% \text{ Inhibition} = \text{A540 Control} - \frac{\text{A540 Extract}}{A540\,Control}$$

Were,
A540 Control- Absorbance of control at 540 nm.
A540 Extract- Absorbance of Extract at 540 nm.

RESULTS AND DISCUSSION

Acute oral toxicity
Swiss albino mice were used in toxicity study. After dosing animals used in toxicity screening, were observed individually for the signs of toxicity. Experimental animals were observed at below mentioned time points during toxicity screening. Once during the first 30 min after AEAM administration. Periodically during the first 24 h of AEAM administration. Special attention was given during the first 4 h after dosing of AEAM. Further animals were observed daily for a total period of 14 days. Observations were made from the signs of toxicity, time of onset of signs of toxicity and length of recovery period. Experimental animals from both vehicles treated and AEAM treated animals were showed no signs of toxicity and showed following observations.

1. No significant changes in behavior.
2. No changes in skin.
3. No changes in breathing pattern.
4. No changes in amount or pattern of food intake as well as water consumption.
5. No change in postural abnormalities.
6. No hair loss.
7. No toxic symptoms or mortality.

Experimental animals were further kept under observation for period of 3 months after AEAM administration. They did not show any sign of toxicity or mortality. AEAM was administered in dose levels of 175 mg/kg, p.o., 550 mg/kg, p.o, 200 mg/kg, p.o of body weight with progression factor of 3.

Oral glucose tolerance test
When compared with normal control group, AEAM fruit peels (400 mg/kg p.o) showed significant decrease in blood glucose level with significant of ($p<0.001$). As compared with control, only Aqueous extract has shown significant increase in glucose level between 30th min and 90th min of oral glucose challenge. This is followed by Metformin-treated group which has shown significant increase in glucose level at 30thmin, as shown in Fig. 1.

Alloxan induced DM
Administration of alloxan (100 mg/kg, i.p.) showed significant ($p<0.01$) increase in serum glucose level on 0th, 7th, and 14th day of observational period, respectively, as compared to the normal group. Administration of Metformin (10 mg/kg, p.o.) showed significant ($p<0.001$) decrease in serum glucose level on 7th and 14th day, respectively (Table 1). Administration of AEAM fruit peels (200 mg/kg, p.o.) showed significant ($p<0.001$) decrease in serum glucose level on 14th day whereas on 7th day, it showed insignificant effect in this regard as compared with control. Administration of AEAM fruit peels (200 mg/kg, p.o.) showed significant ($p<0.001$) decrease in serum glucose level on 14th day, respectively, whereas on 7th day, it showed insignificant effect when compared with standard. Administration of AEAM fruit peels (400 mg/kg, p.o.) showed significant ($p<0.01$) decrease in serum glucose level on 14th day, respectively, as compared with control, as shown in Figs. 2-4.

***In vitro* α-amylase inhibitory activity**
α-amylase inhibitory activity was used to investigate the in-vitro hypoglycaemic activity of the AEAM. Four different concentrations of plant extract were prepared by dissolving in double distilled water. These were 2.5 mg/mL, 5.0 mg/mL, 7.5 mg/mL and 10 mg/mL. Every outcome was contrasted with the common medication Metformin. Out of which concentration at 2.5 mg/mL of AEAM showed 36.3% α-amylase inhibition, 0.5 mg/mL of AEAM showed 45.4% α-amylase inhibitionand 48.48%, 51.5% vice versa. Every outcome was contrasted with the common medication Metformin which showed 69.6% α-amylase inhibition. On comparison of control (vehicle treated group) with standard (Metfomin 1 mg/mL treated group), mean absorbance was significantly ($a<0.05$) reduced. With the increasing concentration

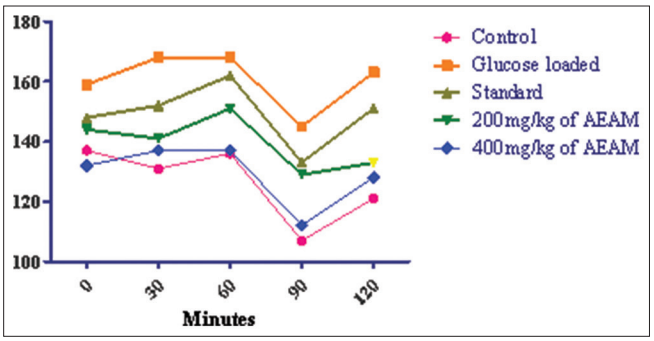

Fig. 1: Effectof AEAM on blood glucose concentrations in fasting conditions at 0 min (pre-treatment) and 30, 60, 90 and 120 min after oral glucose load in normal control mice, and mice treated with various doses of the aqueous fruit peel extract. Every value is shown as mean ± SEM p<0.05 versus glucose loaded control animals at 30 min. p<0.05 versus glucose loaded control animals at 60 min. p<0.05 versus glucose loaded control animals at 90 min. p<0.05 versus glucose loaded control animals at 120 min

Table 1: Effect of AEAM fruit peels on serum glucose level in alloxan induced diabetes mellitus

Group no.	Groups	Serum glucose level		
		0th Day	7th Day	14th Day
I	**Normal**	**82.50±2.963**	**80.17±2.725**	**76.67±2.963**
III	Metformin	188.2±2.87(c z)	163.5±6.276(c)	151.8±9.217(c)
IV	AEAM 200 mg/kg	215.5±4.395(c z)	196.3±6.125(c y)	177.0±5.073(c)
VI	AEAM 400mg/kg	215.8±3.96 (c z)	198.0±4.712(c z)	186.3±7.219(c y)

p<0.05; all data are shown as mean±SEM. versus Normal control animals. p<0.05 versus Diabetic control animals at 7th day, p<0.05 versus 7th day treatment value at 14th day

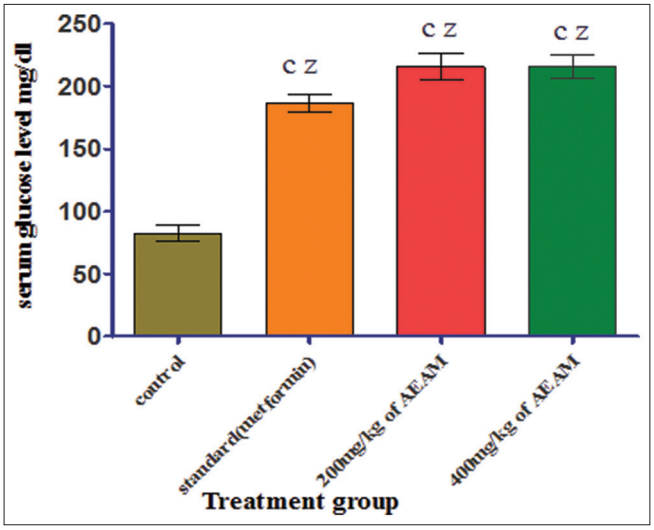

Fig. 2: Effect of AEAM fruit peels on Serum glucose level in alloxan induced diabetes mellitus at day 0. All values are represented as mean±SEM; p<0.05 versus Normal control animals. p<0.05 versus Diabetic control animals at 0th day, p<0.05 versus Test control animals at 0th day

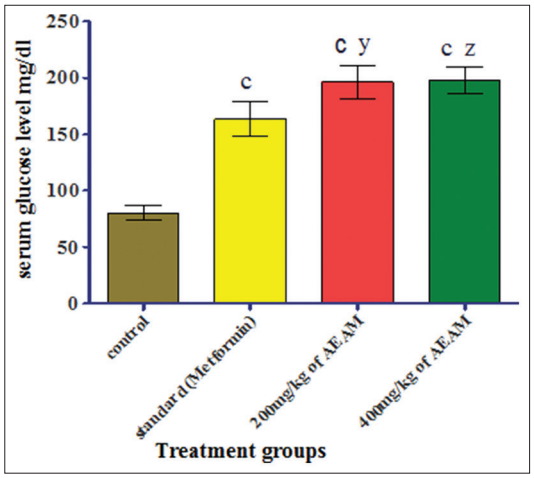

Fig. 3: Effect of AEAM fruit peels on Serum glucose level in alloxan induced diabetes mellitus at day 7th All values are represented as mean±SEM; p<0.05 versus Normal control animals. p<0.05 versus Diabetic control animals at 7th day, p<0.05 versus Test control animals at 7th day

of AEAM fruit peels, increased α-amylase inhibition.as shown in Table 2 and Fig. 5. Hence, hypoglycemic activity of the AEAM fruit peels may be concentration dependent.

Effect of AEAM on % inhibition of α-amylaseat 1.25–10 mg/mL concentrations shows significant change in the absorbance and

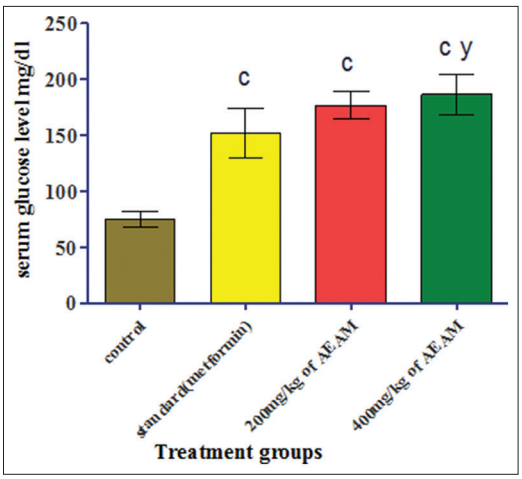

Fig. 4: Effect of AEAM fruit peels on Serum glucose level in alloxan induced diabetes mellitus at day 14th. All values are represented as mean±SEM; p<0.05 versus Normal control animals. p<0.05 versus Diabetic control animals at 14th day, p<0.05 versus Test control animals at 14th day

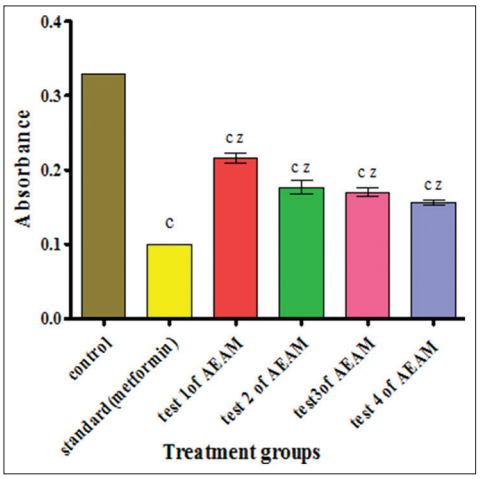

Fig. 5: Percentage inhibition AEAM fruit peels at conc.2.5 mg/mL, 5.0 mg/mL, 7.5 mg/mL and 10 mg/mL. Effect of AEAM on % inhibition of α-amylase at 1.25–10 mg/mL concentrations shows significant change in the absorbance and increases the % inhibition. All values are represented as mean±SEM p<0.05

increases the % inhibition. All values are represented as mean±SEM p<0.05.

Histopathological study observations of pancreas tissue in alloxan-induced diabetes in albino mice

Standard group shows evidence of decrease in necrosis of islets, infiltration of Mononuclear Cells (MNC), reduction in size of islets and

Table 2: Percentage inhibition AEAM fruit peels at concentration2.5 mg/mL, 5.0 mg/mL, 7.5 mg/mL, and 10 mg/mL

S. No.	Group	Concentration (mg/mL)	Absorbance	Mean absorbance	Percent inhibition
1	Control	--	0.35 0.35 0.35	0.33±0.00	--
2	Standard	1.25	0.10 0.10 0.10	0.10±0.00	69.6%
3	Test 1	2.5	0.21 0.23 0.21	0.22±0.006 (c z)	36.3%
4	Test 2	5.0	0.18 0.17 0.16	0.18±0.008 (c z)	45.4%
5	Test 3	7.5	0.18 0.17 0.16	0.17±0.005 (c z)	48.48%
6	Test 4	10	0.16 0.16 0.15	0.16±0.003 (c z)	51.5%

Table 3: Histopathology report of the pancreas tissues in alloxan-induced diabetes mellitus

Groups	Necrosis of islets	Infiltration of MNC	Reduction in size of islets	Acinar cells
Normal	00	00	00	0
Metformin	+	++	++	+
AEAM 200	++	++	++	++
AEAM 400	+	++	+	+

0: no abnormality detected, +: damage/active changes up to <25%, ++: damage/active changes up to <50%, +++: Damage/active changes up to less 75%, ++++: Damage/active changes up to more than 75%

acinar cell degeneration as compare with control. The effect was more prominent on necrosis of islets and acinar cell degeneration. Standard group is composed of lobules formed by acinar structure, each of which is surrounded by connective tissue septa through which run blood vessels, nerves, lymphatics, and interlobular ducts. Number of islets and beta cells are slightly reduced as compare to normal group no evidence of stromal infiltration.

Administration of AEAM fruit peels (200 mg/kg, p.o.) reduces infiltration of MNC. It appeared that the acinar cells were normal. There is a significant lymphocyte infiltration within and around the islets, causing insulinitis. Some normal islet cells are also present magnification 100× the acinar cells are seen to be normal.

Administration of AEAM fruit peels (400 mg/kg, p.o.) reduces infiltration of MNC as well as, it reduces acinar cell degeneration as compare to (200mg/kg p.o).Compared to the control, the islets have a smaller volume but a higher fraction of islet cells. There is very slight inflammatory cell infiltration and no eosinophilic deposits were seen. At magnification 100× the effect was more prominent on reduction in size of islets.

Administration of AEAM fruit peels (400 mg/kg, p.o.) showed reduction in histopathological injury induced by alloxan as evident from decrease in necrosis of islets, infiltration of MNC, reduction in size of islets and acinar cell degeneration as compare with diabetic control. The effect was more prominent on infiltration of MNC, reduction in size of islets and acinar cell degeneration.

Conclusion of histopath study

It was concluded that no pathological changes were observed in control group. Administration of AEAM fruit peels (400 mg/kg, p.o.) showed significantly reduction of the necrosis of islets as indicated by

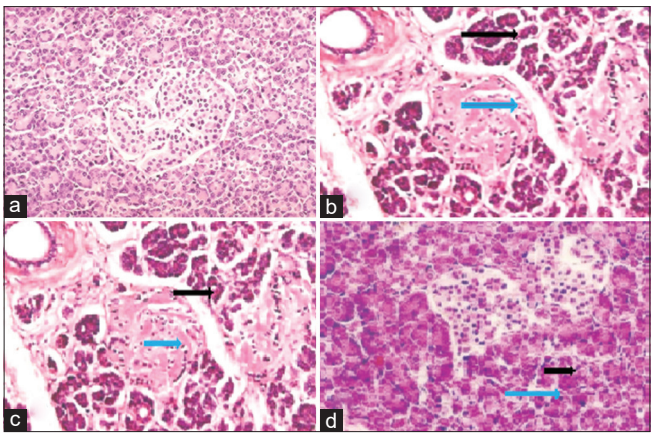

Fig. 6: Histopathological observation of pancreas tissue in alloxan induced diabetes in albino mice. (a) Pancresae section (10×) of control group with very scanty inflammatory cell infiltration and no eosinophilic deposits were seen. (b) Pancrease section (10×) of metformin treated mice, showing necrosis of islets (black arrow), cellular infiltration (blue arrow). (c) Pancrease section (10×) of AEAM fruit peels 200 mg/kg treated mice, showing necrosis of islets (black arrow), cellular infiltration (blue arrow) and small sized islet. (d) Pancrease section (10×) of AEAM fruit peels 400 mg/kg treated mice, showing necrosis of islets (black arrow), cellular infiltration (blue arrow)

significant reduction in the infiltration and acinar cell degeneration, cellular changes as compared to AEAM fruit peels (200 mg/kg, p.o.).

DISCUSSION

AEAM fruit peels have revealed the presence of alkaloids, tannins, flavonoids, phenolic compounds, carbohydrates, glycosides, Vitamin C, saponin, and triterpinoids. Thus, AEAM fruit peels showed hypoglycemic effect due to increased glucose utilization or decreased insulin resistance or increased insulin secretion from β-cells. Glucose (2g/kg) administered orally following 5 h of fasting is best to assess glucose tolerance in mice under these conditions. Hence, AEAM fruit peels show better glucose tolerance at particular time. AEAM fruit peels inhibited the α-amylase activity. As the concentration of dose increases ability of α-amylase inhibition increases. Hence, we can say that inhibition of α-amylase is dose dependent. The protection against the histopathological injury of pancreas, as evident from the decreased inflammation, necrosis and infiltration of MNC in pancreatic tissue,

also revealed the antioxidant potential after induction of AEAM fruit peels.

CONCLUSION

The results of present study concluded that AEAM fruit peels probably by its antioxidant potential prevented the oxidative stress in β-cells, induced by alloxan thereby by preventing the β-cell degeneration and increasing the glucose sensitivity of β-cells leading to increase in insulin release. The effectiveness of AEAM fruit peels in alloxan-induced DM model with its mechanism of action might be due to the presence of flavonoids, alkaloids and tannins or synergistic action of these phytoconstituents. However, the exact role of phytochemicals and their mechanism of action need future investigations.

CONFLICT OF INTERESTS

Declared none.

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