Antidiabetic activity studies of aqueous extract of *Psidium guajava* L leaves on STZ-induced type 2 diabetic model rats

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Introduction

- Type-2 diabetes mellitus become a major global health threat where glucose control on serum remains a major focus in the management of type-2 diabetes [1, 2].
- Alternative strategies for diabetes treatment are urgently required by WHO due to inability of modern therapies to control all pharmacological aspect of this disorder [3].
- An ethno-medicinal plant *Psidium guajava* is commonly known as 'Guava' belongs to myrtaceae family which has been claimed to possess several pharmacological properties including diabetes.
- In Bangladesh different indigenous communities especially the 'Garos' community traditionally uses a combination of seed and fruit of Guava orally for treatment of diabetes mellitus [4].

Fig 1: Psidium guajava leaves

Objective

General Objective

To evaluate the antidiabetic activity of aqueous extract of *P guajava* leaves on streptozotocin induced type 2 diabetic model rats.

Specific Objective

- To explore the effect of *P guajava* leaves extract on glycemic, lipidemic and insulinemic status.
- To explore the mechanism underlying antidiabetic effect.

Materials and Methods

- Fresh leaves of Apple guava (*Psidium guajava*) were collected from available source in Dhaka, Bangladesh and extracted with distilled water. T2DM Long Evans adult rats were developed by induced *ip* (intraperitoneal) injection of STZ to 48 hours old pups and was confirmed with the oral glucose tolerance test (OGTT) after 3 months.

- Experimental rats were divided into four groups (n=7): i) Non-diabetic water control (NDWC) [10 ml/kg bw] ii) Diabetic water control (DWC) [10 ml/kg bw] iii) Gliclazide treated (GT) [20 mg/kg bw] and iv) *Psidium guajava* aqueous extract treated (PGT) [1.25g/kg bw] and the study materials were fed orally for 28 consecutive days.

Fig 2: Experimental design for antidiabetic studies of aqueous extract of *P. guajava* leaves

- Blood samples were collected from tail tip on 0 day and from heart by cardiac puncture on 28th day.

Biochemical Parameters

- Serum glucose was measured by Glucose Oxidase method, Serum insulin was measured by ELISA, Serum lipid was measured by enzymatic-colorimetric method, Liver glycogen content was measured by Anthrone-Sulfuric acid reagent method and Intestinal glucose absorption was measured by gut perfusion technique.

Statistical Analysis

- Data presented as mean±standard deviation (M±SD). Statistical comparison between groups was performed using one way ANOVA and paired t test.

Results and Discussion

- The body weight in different weeks among all the groups of the rats have shown some changes but no significant difference have been found in any of the groups on One way ANOVA and Pair t test respectively.
- Serum glucose level of extract treated group and gliclazide treated group decreased by 16% and 4% respectively where glucose level of water control group increased by 7% on 28 day. But, statistically the reduction of glucose level of PGT and GT was not significant.

Table 1: Chronic effect of aqueous extracts of *P guajava* leaves on fasting serum glucose level of T2DM rats

Group	Fasting serum glucose, mmol/L (M±SD)		
	0 day	14 day	28 day
NDWC (n=6)	5.02±1.22 (100%)	5.36±0.84(106%)	5.41±1.34 (107%)
DWC (n=6)	10.65±2.48(100%)	10.91±3.36(102%)	11.74±3.73 (104%)
GT (n=6)	9.63±2.86 (100%)	9.49±2.96(98%)	9.29±2.61 (96%)
PGT (n=7)	9.12±1.31 (100%)	8.67±0.91(95%)	7.68±0.72(84%)
			p=0.117

Data presented as mean±standard deviation (M±SD). Statistical comparison between groups was performed using one way ANOVA and paired t test. p= 0day vs 28day

- A significant (p<0.05) reduction of LDL-cholesterol level and non-significant increase in HDL-cholesterol (27%) and decrease (40%) in total cholesterol was found in extract treated group compared with the base line value on 28 day but no statistically significant change of lipid profile were found in any other groups.

Fig 3: Chronic effect of aqueous extracts of *P guajava* leaves on Lipid profile level of T2DM rats

Data presented as mean±standard deviation (M±SD). Statistical comparison between groups was performed using one way ANOVA and paired t test. *p and **p= 0 day vs 28 day

- Extract treated group significantly (p<0.05) increased serum insulin whereas other groups showed non-significant effect on serum insulin level when compared with the baseline value on 28 day.

Table 2: Chronic effect of aqueous extracts of *P guajava* leaves on serum insulin level of T2DM rats

Group	Serum Insulin level (µIU/mL)	
	0 day	28 Day
NDWC(n=6)	0.952±0.835 (100%)	1.597±1.117 (167.75%)
DWC(n=6)	0.462±0.312 (100%)	0.304±0.100 (65.80%)
GT(n=6)	0.428±0.464 (100%)	0.367±0.387 (85.74%)
PGT (n=7)	0.319±0.110 (100%)	0.600±0.348(188.08%) *p=0.048

Data presented as mean±standard deviation (M±SD). Statistical comparison between groups was performed using one way ANOVA and paired t test. *p= 0 day vs 28 day.

- Liver glycogen level increase significantly (*p<0.05) of extract treated group in comparison with diabetic water control group on 28 day

Fig 4: Chronic effect of aqueous extracts of *P guajava* leaves on liver glycogen level of T2DM rats

Data presented as mean±standard deviation (M±SD). Statistical comparison between groups was performed using one way ANOVA and paired t test. *p= DWC vs PGT and **p= DWC vs GT.

- Extract treated group significantly (*p<0.05) inhibited glucose absorption from upper intestine.

Table 3: Chronic effect of *P guajava* aqueous extract on Gut perfusion

Solutions	Glucose absorption in upper intestine (mmol/L)	
	Before absorption	After absorption
Krebs	1.32 ± 0.57 (100%)	1.25±0.55 (95%)
Krebs + Glucose	41.17±7.85 (100%)	35.92±17.73 (87%)
Krebs + Glucose + Extract	36.25±8.00 (100%)	34.38±8.40 (95%), *P= 0.039

Data presented as mean±standard deviation (M±SD). Statistical comparison between groups was performed using one way ANOVA and paired t test. *p= before abs vs after abs

Conclusion

- The study revealed that aqueous extracts of *P guajava* leaves possesses antidiabetic activity by stimulating insulin secretion, improving lipidemic status, inhibiting glucose absorption in gut and enhancing glycogenesis in the liver.
- So, based on this result it may conclude that the plants under investigation showed interesting possibilities as a source of oral hypoglycemic agents in diabetic management.

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