Faculty of Education
Department of Biological
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Physiological Studies of Psidium guajava Leaf Extract and Glibenclamide Drug on Streptozotocin Induced Diabetic Male Albino Rats

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Abbreviations	Meaning
DM	Diabetes mellitus
FBGL	fasting blood glucose level
i.p.	intraperitoneal
IP3	Inositol 1,4,5-triphosphate
ER	endoplasmic reticulum
β-cells	beta cells
GIP	glucose-dependent insulinotropic peptide
GLUT2	glucose transporter
IDDM	insulin-dependent diabetes mellitus
PARP	poly ADP-ribose polymerase
K^+	potassium
Ca^{2+}	calcium
NAD^+	Nicotinamide adenine dinucleotide
NIDDM	non-insulin-dependent diabetes mellitus
DKA	diabetic ketoacidosis
HNC	hyperosmolar non-ketotic coma
LA	lactic acidosis
ROS	reactive oxygen species
AGEs	advanced glycation endproducts
TZD	thiazolidinedione
SGLT2	sodium-glucose co-transporter
ATP	adenosine triphosphate
AST	Aspartate Amino Transferase
ALT	Alanine Aminotransferase
ALP	Alkaline Phosphatase
HDL	High Density Lipoprotein
LPL	Lipoprotein Lipase
LDL	Low Density Lipoproteins

Abbreviations	Meaning
GU	guava leaf extract
GLB	glibenclamide
8-OHdG	8-hydroxyl-20-deoxyguanosine
STZ	streptozotocin
P. guajava	*Psidium guajava*
HSCCC method	high-speed counter-current chromatography
WHO	World Health Organization
VLDL	very low-density lipoprotein
PK	protein kinase
NOS	nitrous oxide synthase
K- ATP	ATP-sensitive potassium channels
T2D	Type 2 diabetes
TBA	thiobarbituric acid
HMOX	Heme oxygenase
BLVRA	biliverdin reductase
TBil	total bilirubin
DBil	direct bilirubin
POD	peroxidase
GOD	Glucose oxidase
H_2O_2	hydrogen peroxide
ANOVA	analysis of variance
HIER	heat-induced epitope retrieval

Abstract

The present study was conducted to evaluate the anti-diabetic effect of aqueous extract of guava leaf using streptozotocin–induced diabetic rat. It also compares between the antidiabetic efficacy of guava leaf extract, glibenclamide and their combinations. The present aim was achieved by measuring the serum levels of glucose and insulin together with the histopathological and immunohistochemical changes in pancreatic tissue and insulin content in β cells. The present study extended to investigate the changes in the functions of liver, kidney and lipid profile in the rat model of diabetes, rat model of diabetes treated with guava leaf extract, glibenclamide and their combinations.

Male albino rats were randomly divided into two groups A, B. The first group A served as negative control (n=6) and received daily i.p injections of physiological saline solution (0.9%) for 4 weeks. In the other group (B), rats received a single i.p injection of SZT (60 mg/kg) to obtain the rat model of diabetes. The diabetic rats were further divided into four subgroups (6 each): positive control, diabetic rats treated daily with guava leaf extract (500 mg/ kg, orally), diabetic rats treated

daily with glibenclamide (5 mg/kg, orally) and diabetic rats treated daily with a combination between guava leaf extract (500 mg/kg) and glibenclamide (5 mg/kg) for 4 weeks.

Induction of diabetes in rats by intra peritoneal injection of STZ led to a significant decrease in serum insulin level and a significant increase in blood glucose level. This was associated with a significant increase in AST, ALT, ALP, bilirubin, total cholesterol, triglycerides, LDL, creatinine, urea and uric acid. There were also decreases in the levels of HDL, total protein and albumin as compared with control group. Histological examination of the pancreatic, hepatic and renal tissues showed marked histopathological changes. Immunological changes in pancreatic tissue were observed in diabetic rats induced by STZ. In diabetic rats, pancreatic tissue showed necrosis of the islet tissues, together with moderate congestion of the blood vessels. Liver tissue in diabetic group showed various degrees of pathological changes such as centrilobular fatty degeneration, cloudy swelling as well as necrosis of hepatic cells. The changes in kidney tissue were manifested as shrinkage of Malpighian corpuscles and dilatation of Bowman's space.

When the diabetic group was treated with guava leaf extract, rats showed a control-like insulin level associated with a decrease

in the level of blood glucose. In addition, an improvement in the activities of AST, ALT and ALP and the levels of bilirubin, total cholesterol, triglycerides, LDL, creatinine, urea and uric acid was recorded as compared to the diabetic group. There was an improvement in the levels of HDL, total protein and albumin. Histological examination of the pancreatic, hepatic and renal tissues revealed an improvement of most alterations that were observed in the diabetic rats.

On the other hand, the diabetic group treated with glibenclamide revealed an improvement in serum insulin level and a decrease in the levels of blood glucose level which were less prominent than in case of guava leaf extract treatment. Glibenclamide reduced the elevated activity of ALT and ALP and the elevated levels of total cholesterol, triglycerides, LDL, creatinine, urea and uric acid induced by STZ. However, glibenclamide failed to induce any improvement in AST, bilirubin and HDL level. Histological examination of the pancreas showed an improvement but to a lesser degree than that observed after guava extract. Treatment with glibenclamide showed few pathological changes of the hepatocytes. Glibenclamide improved the changes induced in renal tissue as compared to the diabetic group.