

*Biochemical Changes in Experimental Diabetes
before and after Treatment with Mangifera
indica and Psidium guajava Extracts in Rats*

Presented by

Dawlat Ahmed Sayed

A Thesis Submitted
to
Faculty of Science

In Partial Fulfillment of the
Requirements for
the Degree of
M.Sc. of Science
(Physiology)

**Zoology Department
Faculty of Science
Cairo University
(2010)**

APPROVAL SHEET

Thesis Title

*Biochemical Changes in Experimental Diabetes
Before and After Treatment with
Mangifera indica and Psidium guajava Extracts in Rats*

Name of candidate

DAWLAT AHMED SAYED MOHAMED

Supervision committee

Prof. Dr. Sayed M. Rawi

Professor of general physiology and Neurotoxicity,
Zoology Department,
Faculty of Science, Cairo University

Prof. Dr. Aida M. Saad

Professor of physiology,
The National Organization for Drug Control and Research

Dr. Iman M. Nasef

Lecture of physiology;
Zoology Department, Faculty of Science, Cairo University

Head of Zoology Department

Prof. Dr. Kawthar Abo-Elala

ACKNOWLEDGEMENT

I am deeply thankful to God, by the grace of whom, the present work was realized.

*I wish to express my deep gratitude to **Prof. Dr. Sayed Mohamed Rawi**, Professor of Physiology and Toxicology, Zoology Department, Faculty of Science, Cairo University, for his kindness, encouragement, guidance, patience and supervision. As a supervisor, he makes many suggestions, revised the results and followed the work step by step during the course of this study.*

*I would like to express my deepest gratitude and sincere thanks to Prof. **Dr. Aida M. Saad**, physiology Department in The National Organization for Drug Control and Research for her support and kind encouragement.*

*I offer my deepest and great indebtedness to **Dr. Iman Morad Nasef**, Lecturer of Physiology, Zoology Department, Faculty of Science, Cairo University, for her continuous encouragement, and her supervision.*

*I offer my deepest thanks to **Dr. Adel Bakeer Kholoussy**, Professor of Pathology, Cairo University, for his help and assistance in the histopathology work,*

Finally, my great thanks to my family, for their constant help, patience and encouragement during this study.

LIST OF ABBREVIATION

ALT	: Alanine aminotransferase
ALP	: Alkaline phosphatase
AST	: Aspartate aminotransferase
B.W.	: Body weight
CoA	: Coenzyme A
Diab.	: Diabetic
Diab.-MI	: Diabetic – treated with <i>Mangifera indica</i>
Diab.-PG	: Diabetic – treated with <i>Psidium guajava</i>
Diab.-(MI-PG)	: Diabetic– treated with (<i>Mangifera indica</i> - <i>Psidium guajava</i>)
DNA	: Deoxy-Ribonucleic acid
Fig.	: Figure
GBC	: Glibenclamide
GLUT ₂	: Glucose uptake transporter protein type two
HMG-CoA	: Hydroxymethylglutaryl-Coenzyme A
IDDM	: Insulin dependent diabetes mellitus
MANOVA	: Multi-factor analysis of variance analysis
<i>M. indica</i>	: <i>Mangifera indica</i>
mRNA	: messenger Ribonucleic acids
NADPH	: Nicotinamide adenine dinucleotide phosphate hydrogen
NIDDM	: Non-insulin dependent diabetes mellitus
O.D.	: Optical density
OGTT	: Oral glucose tolerance test
<i>P. guajava</i>	: <i>Psidium guajava</i>
STZ	: Streptozotocin
WHO	: World Health Organization

LIST OF TABLES

	Page
Table (1): Serum glucose level (mg/dl) of diabetic male albino rats before and after treatment with different doses of <i>Mangifera indica</i> water extract post 7 days of continuous daily administration	23
Table (2): Serum glucose level (mg/dl) of diabetic male albino rats before and after treatment with different doses of <i>Psidium guajava</i> water extract post 7 days of continuous daily administration	23
Table (3): Effect of treatment with streptozotocin (50 mg/kg) on body weight gain of male albino rats " <i>Rattus rattus</i> ".	47
Table (4): The effect of oral administration of different plant aqueous extracts and glibenclamide on the body weight gain of STZ-diabetic male albino rats " <i>Rattus rattus</i> "	48
Table (5): Oral glucose tolerance test (OGTT) of normal and diabetic male albino rats.	52
Table (6): Multi-factor Analysis Of Variance (MANOVA) for OGTT of diabetic and diabetic-treated rats at various period of time.	54
Table (7): Effect of oral administration of different plant aqueous extracts and glibenclamide on OGTT of STZ-diabetic male albino rats after one week.	55
Table (8): Effect of oral administration of different plant aqueous extracts and glibenclamide on OGTT of STZ-diabetic male albino rats after two weeks.	56
Table (9): Effect of oral administration of different plant aqueous	58

extracts and glibenclamide on OGTT of STZ-diabetic male albino rats after three weeks.

Table (10): Effect of oral administration of different plant aqueous extracts and glibenclamide on OGTT of STZ-diabetic male albino rats after four weeks.	59
Table (11): Concentration of various biochemical parameters in sera and liver of normal and STZ-diabetic male albino rats " <i>Rattus rattus</i> ".	62
Table (12): Serum insulin concentration (ng/ml) of diabetic and diabetic-treated male albino rats after four weeks of treatments with different plants extracts and glibenclamide.	64
Table (13): Glycogen concentration in liver (mg/g tissue) of diabetic and diabetic-treated male albino rats after four weeks of treatments with different plants extracts and glibenclamide.	65
Table (14): Total protein concentration in serum and liver of diabetic and diabetic-treated male albino rats after four weeks of treatments with different plants extracts and glibenclamide.	68
Table (15): Total lipid concentration in serum and liver of diabetic and diabetic treated male albino rats after four weeks of treatments with different plants extracts and glibenclamide.	71
Table (16): Alkaline phosphatase (ALP) activity in serum and liver of diabetic and diabetic-treated male albino rats after four weeks of treatments with different plants extracts and glibenclamide.	74

Table (17): Alanine aminotransferase (ALT) activity in serum and liver of diabetic and diabetic-treated male albino rats after four weeks of treatments with different plants extracts and glibenclamide.	76
Table (18): Aspartate aminotransferase (AST) activity in serum and liver of diabetic and diabetic-treated male albino rats after four weeks of treatments with different plants extracts and glibenclamide.	79

LIST OF FIGURES

	Page
Fig (1): <i>Psidium guajava</i>	19
Fig (2): <i>Mangifera indica</i>	20
Fig (3): Effect of graded doses of <i>Mangifera indica</i> leaves water extract on blood glucose concentration of STZ diabetic rats after one week of continuous daily administration	24
Fig (4): Effect of graded doses of <i>Psidium guajava</i> leaves water extract on blood glucose concentration of STZ diabetic rats after one week of continuous daily administration.	24
Fig (5): Photomicrograph of pancreatic tissues of normal male albino rat.	34
Fig (6): Photomicrograph of pancreatic tissues of streptozotocin diabetic rat after four weeks.	36
Fig (7): Photomicrograph of pancreatic tissues of streptozotocin diabetic rat treated with glibenclamide after four weeks.	38
Fig (8): Photomicrograph of pancreatic tissues of streptozotocin diabetic rat treated with <i>Mangifera indica</i> extract after four weeks.	40
Fig (9): Photomicrograph of pancreatic tissues of streptozotocin diabetic rat treated with <i>Psidium guajava</i> extract after four weeks.	42
Fig (10): Photomicrograph of pancreatic tissues of streptozotocin diabetic rat treated with mixture of <i>Mangifera indica</i> and <i>Psidium guajava</i> extract after four weeks.	44
Fig (11): Effect of streptozotocin on the body weight of different animal groups of male albino rats.	49

Fig (12): Effect of treatment with different plants extracts and glibenclamide on the body weight gain of STZ-diabetic male albino rats.	49
Fig (13): The oral glucose tolerance curve of normal and diabetic male albino rats at different time interval.	53
Fig (14): Effect of different plants extracts and glibenclamide on glucose tolerance curve of diabetic and diabetic-treated male albino rats at the first week.	57
Fig (15): Effect of different plants extracts and glibenclamide on glucose tolerance curve of diabetic and diabetic-treated male albino rats at the second week	57
Fig (16): Effect of different plants extracts and glibenclamide on glucose tolerance curve of diabetic and diabetic-treated male albino rats at the third week	60
Fig (17): Effect of different plants extracts and glibenclamide on glucose tolerance curve of diabetic and diabetic-treated male albino rats at the fourth week	60
Fig (18): Insulin concentration in serum of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide	66
Fig (19): Glycogen concentration in liver of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide	66
Fig (20a): Total protein concentration in serum of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide	69
Fig (20b): Total protein concentration in liver of diabetic and diabetic-treated rats after four weeks of treatment with different	69

plants extracts and glibenclamide

- Fig (21a):** Total lipid concentration in serum of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide **72**
- Fig (21b):** Total lipid concentration in liver of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide **72**
- Fig (22a):** Alkaline phosphatase (ALP) activity in serum of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide. **75**
- Fig (22b):** Alkaline phosphatase (ALP) activity in liver of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide **75**
- Fig (23a):** Alanine aminotransferase (ALT) activity in serum of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide **77**
- Fig (23b):** Alanine aminotransferase (ALT) activity in liver of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide. **77**
- Fig (24a):** Aspartate aminotransferase (AST) activity in serum of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide. **80**
- Fig (24b):** Aspartate aminotransferase (AST) activity in liver of diabetic and diabetic-treated rats after four weeks of treatment with different plants extracts and glibenclamide. **80**
- Fig (25):** Relative correlation between serum glucose concentration and hepatic glycogen content of treated streptozotocin-diabetic male albino rats. **82**

Fig (26): Relative correlation between insulin level and glucose concentration in serum of treated streptozotocin-diabetic male albino rats.	83
Fig (27): Relative correlation between serum insulin level and hepatic glycogen content of treated streptozotocin-diabetic male albino rats.	83
Fig (28): relative correlation between serum insulin level and serum total proteins of treated streptozotocin-diabetic male albino rats	85
Fig (29): Relative correlation between serum insulin level and hepatic total protein concentration of treated streptozotocin-diabetic male albino rats.	85
Fig (30): Relative correlation between serum insulin level and serum total lipids concentration of treated streptozotocin-diabetic male albino rats.	86
Fig (31): Relative correlation between serum insulin level and hepatic total lipids concentration of treated streptozotocin-diabetic male albino rats.	86
Fig (32): Relative correlation between serum total protein content and ALP activity of treated streptozotocin-diabetic male albino rats.	88
Fig (33): Relative correlation between hepatic total protein content and ALP activity of treated streptozotocin-diabetic male albino rats.	88
Fig (34): Relative correlation between hepatic total protein content and AST activity of treated streptozotocin-diabetic male albino rats.	89
Fig (35): Relative correlation between hepatic total protein content	89

and AST activity of treated streptozotocin-diabetic male albino rats.

Fig (36): Relative correlation between serum total protein content and ALT activity of treated streptozotocin-diabetic male albino rats **90**

Fig (37): Relative correlation between hepatic total protein content and ALT activity of treated streptozotocin-diabetic male albino rats **90**

ABSTRACT

Male adult albino rats were used to study the hypoglycemic effect of *Mangifera indica* and *Psidium guajava* aqueous extracts either used individually or in combination of as well as the effect of glibenclamide as reference sulfonylureas drug at the dose level of 0.5 mg/kg body weight in streptozotocin-diabetic rats. Preliminary test using different doses of each plant indicated that the most effective doses were 250 mg/kg body weight for each plant. Our studies was extended to include the effect of the tested doses on different biochemical parameters including serum insulin concentration, hepatic glycogen content, total proteins, total lipids and transaminases activities in serum and liver. In addition to the previously investigated analysis our study was also extended to include the histopathological effect of the tested materials on the pancreatic cells of STZ-diabetic rats.

The obtained data of the above mentioned investigations revealed great alleviation of the impaired glucose tolerance, serum insulin and hepatic glycogen content, also serum and hepatic total protein contents were increased as a result of treatment.

In STZ-diabetic rats, the activities of (ALT, AST and ALP) either detected in sera or hepatic tissues were increased, then the activities were improved as a result of treatments.

Also, the islets of Langerhans of STZ-diabetic rats showed vaculation and hydropic degeneration of many cells and the treatments stimulate the rate of recovery of the islet cells.

Key words:

Hypoglycemic, Streptozotocin, *Mangifera indica* and *Psidium guajava*

CONTENTS

	Page
INTRODUCTION.....	1
AIM OF WORK.....	4
REVIEW OF LITERATURE.....	5
MATERIALS AND METHODS.....	17
RESULTS.....	32
(I) Histopathological effects	32
(II) Effect of treatment on body weight gain.....	46
(III) Effect on oral glucose tolerance test (OGTT).....	50
(IV) Biochemical effects.....	61
(A) Concentration of various biochemical parameters in sera and liver of normal and diabetic male albino rats "<i>Rattus rattus</i>".....	61
(B) Effect of treatment with the tested materials and glibenclamide on various biochemical parameters in sera and liver of diabetic male albino rats "<i>Rattus rattus</i>".....	63
(1) Serum insulin concentration	63
(2) Liver glycogen concentration.....	63
(3) Total protein concentration.....	67
(4) Total lipid concentration.....	70
(5) Alkaline phosphatase activity.....	73
(6) Alanine aminotransferase (ALT) activity.....	73
(7) Aspartate aminotransferase (AST) activity.....	78
(V) Relative correlations.....	81
(A) Glucose & Glycogen Correlation	81
(B) Correlation between insulin and glucose, glycogen, total proteins and total lipids.....	81
(1) Insulin-glucose & insulin-glycogen correlations.....	81
(2) Insulin-total proteins correlation.....	84
(3) Insulin-total lipids correlation.....	84
(C) Correlation between total proteins and enzyme activities:	87

(1) Total proteins-ALP activity.....	87
(2) Total proteins-AST activity.....	87
(3) Total proteins-ALT activity.....	87
DISCUSSION.....	91
SUMMARY.....	111
REFERENCES.....	115