An evaluation of anti-diabetic and anti-lipidemic properties of *Momordica Charantia* (Bitter melon) fruit extract in experimentally induced diabetes.

A thesis

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بسم الله الرحمن الرحيم

"سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم"

صدق الله العظيم

الآيه 32 من سورة البقرة

To the Most Kind
and Gracious Person
in the World

My Husband

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Madeha Ali Ewais

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LIST OF ABBREVIATIONS

A: Absorbance.
ADA: American Diabetes Association.

ADP: Adenosine diphosphate.

ALT: Alanine aminotransferase.

ANOVA: analysis of variance.

AP: Alkaline phosphatase.

AST: Aspartate aminotransferase.

BM: Bitter melon.

C: centigrade.

CD: Cluster of differentiation.

DAV: Diabetic received avandia.

DBM: Diabetic received bitter melon.

DC: Diabetic control.

DNA: Deoxy nucleic acid.

E: Extintion.

EDTA: Ethylenediamine tetraacetic acid.

FPG: Fasting plasma glucose.

G-6-P: Glucose 6-phosphate.

G-6-Pase: Glucose-6-phosphatase.

GAGs: Glycosaminoglycans.

GI: Glycemic index.

GIP: Glucose dependent insulinotropic peptide.

GLP-1: Glucagon-like peptide-1.

GLUT: Glucose transporter.

Gly. Hb A1: Glycohemoglobin.

Hb: Hemoglobin.

HDL: High density lipoprotein**.**

IFG: Impaired fasting glucose.

IGT: Impaired glucose tolerance.

KDa: Kilo dalton.

LDL: Low density lipoproteins.

LSD: least significance difference.

M.charantia: Momordica charantia.

mg/kg B.Wt: Milligram per kilogram body weight.

NBM: Normal received bitter melon**.**

NC: Normal control.

NO: Nitric oxide.

OGTT: Oral glucose tolerance test.

P: propability.

PI3K: Phosphatidyl inositol 3 kinase**.**

PPARγ: Peroxisome proliferator-activated receptor γ.

RDA: Recommended daily allowance.

RNA: Ribonucleic acid.

S.D: standard deviation.

T2DM: Type 2 diabetes mellitus**.**

U.S.A: United States of America.

U/l: Unit per litre.

VIP: Vasoactive intestinal peptide.

VLDL: Very Low density lipoproteins.

ABSTRACT

The current study was done to investigate the anti-diabetic and anti-lipidemic properties of momodica charantia(bitter melon) fruit extract in alloxan diabetic rats treated for 4 weeks.

At the end of the experimental period, several studies were performed including oral glucose tolerance test, serum insulin, blood glycated hemoglobin, liver glycogen, ALT, AST, lipid profiles to demonstrate the anti-diabetic and ant-lipidemic effect, in addition to in vitro and insitu studies as well as histopathological study to the suggest the possible mechanism of action of the plant.

An oral hypoglycemic drug, rosiglitazone was used for comparison with bitter melon.

Conclusion, bitter melon had a significant hypoglycemic an hypolipidemic effects when compared to rosiglitazone and this could be due to increase insulin release, increase glucose uptake and decrease glucose absorption.

Key words: bitter melon – rats – alloxan- diabetes.


Introduction

INTRODUCTION

Diabetes mellitus is the most common endocrine disease. It affected 2-3% of the total world population in 2001(***Alberti et al., 2002***). Diabetes mellitus leads to metabolic abnormalities and is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both (***Fonseca et al., 2000***).

Although, oral hypoglycemic agents and insulin are the mainstay of treatment of diabetes and are effective in controlling hyperglycemia, they have prominent side effects and fail to significantly alter the course of diabetic complications (***Maghrani et al., 2004***).

The common side effects associated with oral hypoglycemic agents are hypoglycemia, weight gain, gastrointestinal disorders, peripheral edema and impaired liver function (***Mallare et al., 2005***). In addition, the cost of treatment has also become a real concern.

Since natural remedies are somehow safer and more efficacious than remedies that are pharmaceutically derived, herbalism has become mainstream worldwide ***(Bateman et al., 1998 and Murphy, 2000).***

In this study, we have taken a targeted approach to investigate the anti-diabetic properties of ***Momordica charantia***, also known as bitter melon, bitter gourd, or balsam pear.

Bitter melon is a plant widely cultivated in many tropical and subtropical regions of the world and is frequently used in South Asia and the Orient as a

food stuff and medicinal plant. Extracts from various components of this plant have been reported to possess hypoglycaemic activity (***Lin et al., 1999; Barbieri et al., 1999 and Karunanayake et al., 2003***), anti-tumour (***Clafin et al., 2002 and Jilka et al., 2003)***, and abortifacient properties (***Morton, 2007***).

Momordica charantia fruit juice has been shown to increase *both glucose uptake by tissues and liver glycogen storage* (***Welihinda et al., 2006).*** The freeze-dried juice of ***Momordica charantia*** can also stimulate insulin secretion by *beta* cells of the islets of Langerhans (***Welihinda et al., 2005).***

The hypoglycemic activity of ***Momordica charantia*** fruit juice is demonstrated in animals with experimental diabetes (***Day et al., 2000 and Karunanayake et al., 2004)*** and also in humans in both type 1 and type 2 diabetes mellitus (***Baldwa et al., 1997; Leatherdale et al., 2001 and Welihinda et al., 2006).***

Aim of work

AIM OF WORK

The present study aims at investigating the effect of ***momordica charantia*** (bitter melon) fruit extract compared to rosiglitazone maleate, an oral hypoglycemic drug, on glucose tolerance and some biochemical parameters in alloxan induced diabetes, and to suggest the possible mechanisms of the hypoglycemic action of such agents through the followings:

1-Induction of diabetes mellitus by alloxan.

2-Preliminary testing of hypoglycemic activity of different doses of bitter melon for 1 week using mild diabetic rats to select the most potent dose which was used in the subsequent studies.

3-Effect of alloxan induced diabetes as well as rosiglitazone maleate and ***momordica charantia*** treatments on:

(a) Body weight.

(b) Oral glucose tolerance test.

(c) Serum insulin.

(d) Blood glycohemoglobin [Gly.HbA1] percentage.

(e) Liver glycogen content.

(f) Serum ALT and AST.

(g) Serum lipid profiles (triglycerides, total cholesterol, LDL-