بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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MONA MAGHRABY

Serum Glucagon like peptide 1 Level and Peripheral Vascular Disease in Patients with Type 2 Diabetes

Thesis
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In Endocrinology and metabolism

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بِسْمِ اللَّـهِ الرَّحْمَـٰنِ الرَّحِيمِ

فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَى إِلَيْكَ وَحْيُهُ

وَقُلْ رَبِّ زِدْنِي عِلْمًا

طه.(114)

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List of Abbreviations

2HPPG	2 hours postprandial glucose
ABI	Ankle-brachial index
AC	adenylate cyclase
AGEs	advanced glycation end products
AIDS	Acquired immunodeficiency syndrome
ALI	Acute limb ischemia
AMPK	adenosine monophosphate activated protein kinase
APSV	ankle peak systolic velocity
ASCVD	Atherosclerotic cardiovascular disease
ATII	angiotensin II
ATP	adenosine tri phosphate
BBB	blood brain barrier
BID	twice daily
CAD	coronary artery disease
cAMP	cyclic adenyl monophosphate
cGMP	cyclic guanosine monophosphate
CICR	calcium-induced calcium release
CLI	critical limb ischemia
CNS	central nervous system
CVD	cardiovascular disease
DM	diabetes mellitus
DPP-4	dipeptidylpeptidase-4

ECD	Endothelial cell dysfunction
ECs	endothelial cells
EECs	enteroendocrine cells
eNOS	endothelial nitric oxide synthase
Epac2	exchange protein activated by cAMP
FBG	fasting blood glucose
GDM	Gestational diabetes
GHRH	growth hormone releasing hormone
GIP	glucose- dependent insulino-tropic polypeptide.
GLP- 1R	glucagon like peptide 1 receptor
GLP 2	Glucagon Like Peptide 2.
GLP-1	glucagon-like peptide 1.
GLUT1/2	glucose transporter 1/2
GRPP	glicentin-related polypeptide
hbA1C	glycated hemoglobin
HIF	hypoxia inducible factor
HIV	human immunodeficiency virus
hVECs	human vascular endothelial cells
IC	intermittent claudication
ICAM-1	intracellular adhesion molecule1
IELs	Intestinalintraepithelial lymphocytes
IL-1	interleukin-1
IP-1	intervening peptide-1
IP-2	intervening peptide-2
MCP-1	Monocyte Chemattractant protein-1
MEG-1	megakaryocyte-1

MI	myocardial infarction
MODY	maturity-onset diabetes of the young
MPGF	major proglucagon fragment
MRA	magnetic resonance angiography
mRNA	messenger ribonucleic acid
NF-KB	nuclear factor kappa B
NO	nitric oxide
NSGP	National Glycohemoglobin Standardization Program
NTS	nucleus tractus solitari
OGTT	oral glucose tolerance test
PAD	peripheral arterial disease
PAI-1	plasminogen activator inhibitor-1
PC1/3	prohormone convertase 1/3
PC2	prohormone convertase2
PCSK1	prohormone convertase subtilisin-kexin 1
PCSK2	prohormone convertase subtilisin-kexin 2
PDR	proliferative diabetic retinopathy
Pdx-1	pancreatic and duodenal homeobox 1
PG	prostaglandin
PI3K	phosphatidylinositol-3 kinase
PKA	protein kinase A
PKB	protein kinase B
PTH	parathyroid hormone
PVD	peripheral vascular disease
QW	once weekly

RAGE	Receptor for advanced glycation end products
ROS	reactive oxygen species
SGLT2	sodium glucose transporter 2
SIRT6	sirtuin6
SMCs	smooth muscle cells
TBI	tibial-brachial index
TcPO2	Transcutaneous Oxymetry
TF	tumor necrosis factor
TNFα	tumour necrosis factor α
VAM	vascular adhesion molecule
VCAM-1	vascular cell adhesion molecule 1
VECs	Vascular Endothelial Cells
VEGF	vascular endothelial growth factor
VSMCs	Vascular Smooth Muscle Cells
WBCs	white blood cells

Introduction

Introduction

Diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control ***(Grant and Kirkman, 2015).***

GLP-1 is synthesized and secreted from enteroendocrine L cells found throughout the small and large intestine. GLP-1 increases insulin and inhibits glucagon secretion in a glucose-dependent manner. GLP-1 also stimulates beta cell proliferation and neogenesis, and inhibits beta cell apoptosis ***(Jonathan et al., 2013).***

GLP1 has several actions in both diabetics and healthy individuals, mediated through receptor (GLP1-R) which is present abundantly in endothelial cells and vascular smooth muscle cells ***(Sleiman and Azar ,2012).*** Recently both GLP1 and its metabolite were found to have a glucose independent vasorelaxant effects ***(Sleiman and Azar ,2012).***

Peripheral arterial disease (PAD) in people with type 2 diabetes mellitus (T2DM) exhibits broad clinical characteristics and various consequences and is known as one of the major macrovascular complications of T2DM, the prevalence of which is on the rise. Atherosclerosis is recognized as the most direct and important cause of PAD ***(Sang and Young, 2015).***

Ankle Peak Systolic Velocity (APSV) is the mean of the peak systolic velocities measured across the distal tibial arteries at the ankle level during arterial duplex scanning of the lower extremities ***(Bishara, et al., 2009).***