

شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو

بسم الله الرحمن الرحيم





MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكترونى والميكروفيلم

جامعة عين شمس التوثيق الإلكتروني والميكروفيلم قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY

The Effect of Intermittent Fasting on Isoproterenol-Induced Myocardial Infarction in Aged Rats: A Potential Role of Autophagy

Thesis

Submitted For Partial Fulfillment of Master Degree in Basic Medical Science (Physiology)

Presented by Aya Ahmed Hanafy

M.B.B.Ch Faculty of Medicine – Ain Shams University

Under Supervision of

Prof. Sahar Mohamed El Agaty

Professor of Physiology Faculty of Medicine – Ain Shams University

Dr. Noha Abdel-Aziz Nassef

Assistant Professor of Physiology Faculty of Medicine – Ain Shams University

Dr. Doaa Ahmed Abou-Bakr

Assistant Professor of Physiology Faculty of Medicine – Ain Shams University

Department of Medical Physiology Faculty of Medicine – Ain Shams University 2021

Acknowledgement

First and foremost, Thanks to **Allah** for His showers of blessings to complete this research work or any work in my life successfully.

I would like to express my deep gratitude and sincere appreciation to **Prof. Dr. Sahar Mohamed El Agaty**, Professor of Physiology, Faculty of Medicine- Ain Shams University for her valuable instructions, her endless patience with me and for unlimited help and great deal of support. Her vision and motivation have deeply inspired me and her experienced guidance made the completion of this work possible.

I owe special feeling of gratitude to **Dr. Noha Abdel-Aziz Nassef**, Assistant Professor of Physiology, Faculty of Medicine- Ain Shams University for her great help, close supervision, wise opinions, guidance and her continuous encouragement and for her precious effort. It was a great privilege and honor to do this thesis under her supervision.

My deep appreciation to **Dr. Doaa Ahmed Abou-Bakr**, Assistant Professor of Physiology, Faculty of Medicine- Ain Shams University for her sustained support, helpful suggestions and for her precious time and effort that made this thesis possible.

I am also grateful to **Prof. Dr. Nermine Kamal Mohamed**, Professor and Head of Physiology Department, Faculty of Medicine- Ain Shams University, for her unique effort, and considerable help throughout this work.

I am also grateful to **Dr. Sayed Abdel Raheem**, Assistant Professor of Histopathology, Faculty of Medicine- Al Azhar University, for his contribution in the histological studies.

I also want to thank **Dr. Laila Ahmed Rashed**, Professor of Medical Biochemistry and Molecular Biology, Faculty of Medicine- Cairo University, for her contribution in the biochemical analysis.

Last but not least, I dedicate this work to **my family**, whom without their sincere support, and prayers, this work would not have been completed.

Aya Ahmed

Contents

Subject Pages No.
List of Abbreviations
List of TablesV
List of FiguresXIII
Introduction1
Aim of the Work
Review of Literature5
1 Aging 5
 Aging
3. The effect of aging on adipose tissue8
4. The effect of aging on lipid metabolism9
5. The effect of aging on glucose homeostasis
6. The role of oxidative stress in age related cardiovascular
changes
7. The role of inflammation in age related cardiovascular
changes
8. The effect of aging on autophagy in cardiac muscle14
9. Intermittent Fasting
10. The effect of intermittent fasting on cardiovascular function
17
11. The effect of intermittent fasting on adipose tissue20
12. The effect of intermittent fasting on lipid metabolism21
13. The effect of intermittent fasting on glucose homeostasis
22
14. The effect of intermittent fasting on oxidative stress23
15. The effect of intermittent fasting on inflammation24
16. The effect of intermittent fasting on autophagy26

Subject	Pages No.
Materials and Methods	28
Results	68
Discussion	129
Summary and Conclusion	142
References	148
Arabic Summary	

List of Abbreviations

Abb.	Full Term
% BMI	percentage change in body mass index
% BW	percentage change in body weight
% WC	percentage change in waist circumference
AI	Atherogenic index
AMPK	Adenosine monophosphate-activated protein
	kinase
ANOVA	Analysis of variance
Atg-5	Autophagy related protein-5
Atg-7	Autophagy related protein-7
BDNF	Brain-derived neurotrophic factor
BL	Body length
BMI	Body mass index
BMI_i	Initial body mass index
$\mathbf{BMI_f}$	Final body mass index
\mathbf{BW}	Body weight
BW_i	Initial body weight
$\mathbf{BW_f}$	Final body weight
CK-MB	Creatine Kinase- Myocardial Band
CRP	C-Reactive protein
cTnI	Cardiac troponin-I
eNOS	Endothelial nitric oxide synthase

Abb.	Full Term
FOXO	Forkhead box O transcription factor
FPG	Fasting plasma glucose
FFAs	Free fatty acids
FI	Fasting insulin
GIP	Glucose-dependent insulinotropic polypeptide
GSH	Reduced glutathione
GSSG	Oxidized glutathione
H&E	Hematoxylin & Eosin
HDL-C	High density lipoprotein cholesterol
HOMA-%B	Homeostatic model assessment of beta-cell function
HOMA-IR	Homeostatic model assessment of insulin resistance
IF	Intermittent fasting
IL	Interleukins
ISO	Isoproterenol
LAMP2	Lysosomal associated membrane protein 2
LC3	Microtubule-associated protein 1A/1B light chain
	3
LDL-C	Low density lipoprotein cholesterol
LI	Liver index
LV	Left ventricle
LW	Liver weight

Abb. Full Ter	m
---------------	---

MDA Malondialdehyde

MI Myocardial infarction

mTOR Mammalian target of rapamycin

NADPH Reduced form of nicotinamide adenine

dinucleotide phosphate

NF- kB Nuclear factor kappa B

NO Nitric oxide

O.D. Optical density

Old-F Old group subjected to intermittent fasting

Old-F-ISO Old group subjected to intermittent fasting and

treated by isoproterenol

Old-ISO Old group treated by isoproterenol

PF Periodic fasting

ROS Reactive oxygen species

SASP Senescence- associated secretory phenotype

SIRT Silent information regulator

SPSS Statistical Program for Social Science

TC Total cholesterol

TRF Time restricted feeding

TFEB Transcription factor EB

TGs Triglycerides

TGF-β1 Transforming growth factor beta-1

TNF-alpha Tumor necrosis factor- alpha

Abb.	Full Term
ULK1	Unc-51 like autophagy activating kinase-1
VATW	visceral adipose tissue weight
VLDL	Very low density lipoprotein
WC	Waist circumference
WC_i	Initial waist circumference
WC_f	Final waist circumference

List of Tables

Table	Title	Page
1	The primer sequence of the studied genes.	63
2	Running condition for RT-PCR.	64
3	Changes in initial body weight (BW_i) , final body weight (BW_f) , and the percentage change in body weight $(\%\ BW)$, in the five study groups.	71
4	Changes in initial body mass index (BMI_i) , final body mass index (BMI_f) , and the percentage change in body mass index (% BMI), in the five study groups.	72
5	Changes in initial waist circumference (WC $_{\rm i}$), final waist circumference (WC $_{\rm f}$), and the percentage change in waist circumference (% WC), in the five study groups.	73
6	Changes in visceral adipose tissue weight (VATW) and visceral adipose tissue weight/body weight (VATW/BW), in the five study groups.	74
7	Changes in fasting plasma glucose (FPG), plasma level of fasting insulin (FI), and mRNA expression of pancreatic autophagy related protein-7 (Atg-7), in the five study groups.	81
8	Changes in Homeostatic model assessment of insulin resistance (HOMA-IR), and Homeostatic model assessment of beta-cell function (HOMA-%B), in the five study groups.	82

Table	Title	Page
9	Changes in plasma levels of triglycerides (TGs), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C) in the five study groups.	87
10	Changes in atherogenic index (AI), liver weight (LW), and liver index (LI) in the five study groups.	88
11	Changes in plasma level of troponin-I (Troponin-I), and Creatine Kinase-Myocardial Band (CK-MB), in the five study groups.	93
12	Changes in cardiac level of malondialdehyde (MDA), reduced glutathione (GSH), tumor necrosis factor- alpha (TNF-alpha), and cardiac mRNA expression of autophagy related protein-5 (Atg-5), in the five study groups.	97
13	Initial body weight (BW_i) , final body weight (BW_f) , the percentage change in body weight $(\% BW)$, initial body mass index (BMI_i) , final body mass index (BMI_f) , and the percentage change in body mass index $(\% BMI)$, in adult group.	104
14	Initial body weight (BW_i) , final body weight (BW_f) , the percentage change in body weight $(\% BW)$, initial body mass index (BMI_i) , final body mass index (BMI_f) , and the percentage change in body mass index $(\% BMI)$, in old group.	105

Table	Title	Page
15	Initial body weight (BW _i), final body weight (BW _f), the percentage change in body weight (% BW), initial body mass index (BMI _i), final body mass index (BMI _f), and the percentage change in body mass index (% BMI), in old-intermittent fasting group.	106
16	Initial body weight (BW_i) , final body weight (BW_f) , the percentage change in body weight $(\% BW)$, initial body mass index (BMI_i) , final body mass index (BMI_f) , and the percentage change in body mass index $(\% BMI)$, in old-isoproterenol group.	107
17	Initial body weight (BW_i) , final body weight (BW_f) , the percentage change in body weight $(\% BW)$, initial body mass index (BMI_i) , final body mass index (BMI_f) , and the percentage change in body mass index $(\% BMI)$, in old-intermittent fasting-isoproterenol group.	108
18	Initial waist circumference (WC _i), final waist circumference (WC _f), the percentage change in waist circumference (% WC), visceral adipose tissue weight (VATW), and visceral adipose tissue weight/body weight (VATW/BW), in adult group.	109
19	Initial waist circumference (WC _i), final waist circumference (WC _f), the percentage change in waist circumference (% WC), visceral adipose tissue weight (VATW), and visceral adipose tissue weight/body weight (VATW/BW), in old group.	110