Effects of Taurine Supplementation on Biomarkers of Oxidative Stress in Insulin-Resistant Rats.

A thesis submitted for partial fulfillment of master degree in pharmaceutical science (Biochemistry)

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2010

Acknowledgment

First and foremost, Thanks are due to **Allah.**

I am much honored to be supervised by **Prof. Dr. Hala El-Mesallamy**, Head of Biochemistry Department, and Vice Dean for community and environmental affairs, Faculty of Pharmacy, Ain-Shams University, who has put the idea of the research and designed the protocol of the study. I would like to thank her for enlightening me with her thoughts, her valuable supervision, and her general encouragement. I would like to thank her for the vital assistance and motivation she has extended.

Words cannot express my deep gratitude and sincere appreciation to **Dr. Lamiaa N Hammad**, Acting Head of Biochemistry Department, Faculty of Pharmacy, Misr International University. I would like to thank her for her close follow up and tangible efforts throughout the experimental work, her step by step assistance in collecting the required samples, as well as analyzing them, and for her superb guidance during writing the manuscript.

I would like to extend my cordial appreciation to **Dr. Ebtehal El-Demerdash**, Acting Head of Pharmacology & Toxicology Department, Faculty of Pharmacy, Ain-Shams University, for her generous help and guidance during the experimental work and data analysis, as well as her valuable participation in revising the manuscript.

I would like to convey my special thanks to Misr International University (MIU), for without its equipped research lab, animal house,

library, and financial support, I could have never been able to finish my study.

I would like to thank all MIU staff members who supported me to accomplish my goal all along the way. They offered me knowledge, persistence, encouragement, and assistance whenever needed.

Furthermore, I would like to thank US NAMRU-3, Cairo, Egypt for their cooperation, as well as kind receptiveness.

I would like to extend my gratefulness to my parents, who provided me with prayers and support at every moment of my life, to my husband who stood beside me all along the road, and to my little angel.

Last but not the least; I would like to express my heartfelt feelings towards my MIU colleagues who were willingly overloaded by much work to help me finish my research.

List of Abbreviations

4-AP	4-aminophenazone.
ACAT	Acyl-CoA: cholesterol acyltransferase
ADMA	Asymmetrical dimethylarginine.
ADP	Adenosine diphosphate.
A-FLIGHT toxicities	The manifold toxicities associated with insulin resistance, metabolic syndrome and type 2 diabetes mellitus.
AGEs	Advanced glycation end-products.
AMP	Adenosine monophosphate.
ANG II	Angiotensin II.
ATP	Adenosine triphosphate.
AUC	Area under the curve.
BH_4	Tetrahydrobiopterin.
bHcy	Protein bound homocysteine.
BHMT	Betaine:homocysteine methyltransferase.
BMI	Body mass index.
CAD	Coronary artery diseases.
cAMP	Cyclic adenosine monophosphate.
CDO	Cysteine dioxygenase.
cGMP	Cyclic guanosine monophosphate.
CHE	Cholesterol esterase enzyme.
CHOD	Cholesterol oxidase enzyme.
CMIA	Chemiluminescent microparticle immunoassay.
CRP	C-reactive protein.
CSAD	Cysteine sulfinic acid decarboxylase.
CVD	Cardiovascular diseases
CβS	Cystathionine β synthase.
DAG	Diacyl glycerol.
DHAP	Dihydroxyacetone phosphate
DNA	Deoxyribonucleic acid.
DTT	Dithiothreitol.
EDTA	Ethylene diamino tetraacetic acid.
ELISA	Enzyme linked immunosorbent assay.
eNO	Endothelial nitric oxide.
eNOS	Endothelial nitric oxide synthase.
ET-1	Endothelin-1.
exSOD	Extracellular superoxide dismutase.
FFA	Free fatty acids.

G-6-PDH	Glucose-6-phosphate dehydrogenase
GABA	γ-aminobutyric acid.
GI	Glycemic index.
GK	Glycerol kinase.
GLUT	Glucose transporter.
GOD	Glucose oxidase.
GPO	Glycerol-3-phosphate oxidase.
GPx	Glutathione peroxidase.
GSH	Glutathione (reduced).
GSSG	Glutathione (oxidized)
H_2O_2	Hydrogen peroxide.
HCl	Hydrochloric acid.
Hcy	Homocysteine.
Hcy-Cys	Homocysteine-Cysteine.
HcyH	Free homocysteine.
Hcy-Hcy	Homocysteine-Homocysteine.
HcyT	Homocysteine thiolactone.
HDL	High density lipoprotein.
HDL-C	Human hepatoblastoma.
Hep G2	Human hepatoblastoma.
HFCS	High fructose corn syrups.
HHcy	Hyperhomocysteinemia.
HMG-CoA reductase	3-hydroxy-3-methylglutaryl-coenzymeA reductase.
HMP	Hexose monophosphate.
HNO_2	Nitrous oxide.
HOCl	Hypochlorous acid.
HOMA-IR	Homeostasis model assessment of insulin resistance.
$HRO_2\bullet^-$	Hydroperoxyl.
HRP	Horseradish peroxidase.
IDL	Intermediate density lipoproteins.
IL-6	Interleukin 6.
iNOS	Inducible nitric oxide synthase.
IR	Insulin resistance.
IRS	Insulin receptor substrate.
JNK	c-jun N-terminal kinase
kDa	Kilo dalton.
LCAT	Lecithin:cholesterol acyl transferase
LDL	Low density lipoprotein.
LDL-C	Low density lipoprotein cholesterol.

LDLR	Low-density lipoprotein receptor
L-NMMA	NG-monomethyl-L-arginine.
LPL	Lipoprotein lipase.
MAPK	Mitogen activated protein kinase.
MnSOD	Mitochondrial superoxide dismutase.
mRNA	Messenger ribonucleic acid.
MS	Metabolic syndrome.
MTHFR	Methylenetetrahydrofolate reductase.
$NADH+H^+$	Nicotinamide adenine dinucleotide (reduced).
$NADPH+H^+$	Nictotinamide adenine dinucleotide phosphate (reduced)
NCEP-ATP III	National Cholesterol Education Program's Adult Treatment Panel III
NEDD	N-(1-naphthyl) ethylenediamine dihydrochloride.
NF-kB	Nuclear factor kappa B.
NNMT	N-nictotinamide methyltransferase.
nNOS	Neuronal nitric oxide synthase.
NO	Nitric oxide.
NOS	Nitric oxide synthase.
NOx	Nitric oxide metabolites.
$O_2•^-$	Superoxide.
OGTT	Oral glucose tolerance tests.
OH•	Hydroxyl.
OLETF rats	Otsuka Long-Evans Tokushima Fatty rats.
$ONOO^-$	Peroxynitrie.
PGI_2	Prostacyclin I_2.
PI3K	Phosphatidylinositol-3-kinase.
PKC	Protein kinase C.
POD	Peroxidase enzyme.
PON	Paraoxonase enzyme.
QC	Quality control.
QUICKI	Quantitative insulin-sensitivity check index.
RLU	Relative light units.
RNS	Reactive nitrogen species.
$RO_2•$	Peroxyl.
RONOO	Peroxynitrate.
ROS	Reactive oxygen species.
SAC	S-adenosyl cysteine.
SAH	S-adenosyl homocysteine.
SAHHase	S-adenosyl homocysteine hydrolase.

SAM	S-adenosyl methionine.
SOD	Superoxide dismutase.
SREBP-1c	Sterol regulatory element binding protein-1c.
T1DM	Type 1 diabetes mellitus.
T2DM	Type 2 diabetes mellitus.
TAC	Total antioxidant capacity.
TauT	Taurine transporter.
T-Chol	Total cholesterol.
TGs	Triglycerides.
tHcy	Total homocysteine.
TNF-α	Tumor necrosis factor alpha.
TxA_2	Thromboxane A_2.
UDP	Uridine diposphate.
VCl_3	Vanadium trichloride.
VLDL-C	Very low density lipoprotein cholesterol.

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Aim of the Work

Rats fed a high-fructose diet develop a cluster of abnormalities including hyperinsulinemia, glucose intolerance and hypertension. In addition, prolonged fructose treatment affects lipid metabolism and causes alterations in plasma lipid profile ***(Nandhini et al., 2002a).*** Fructose fed rats form a useful experimental model of insulin resistance (IR). Moreover, fructose feeding is reported to facilitate oxidative damage and has deleterious effects both due to reduction in antioxidant defense and enhanced free radical production ***(Busserolles et al., 2002).***

The IR observed in the fructose fed-rat model may be attributed to a low level of insulin stimulated glucose uptake and oxidation in skeletal muscles and adipose tissues due to modification in the post receptor cascade of insulin action ***(Catena et al., 2003).***

Hyperglycemia results in low density lipoprotein (LDL) being seeded with small amounts of lipid peroxides rendering it more susceptible to oxidation. Oxidative modification of LDL is implicated in the pathogenesis of many vascular diseases in fructose-induced insulin resistant animals ***(Kopprasch et al., 2002).*** High density lipoprotein (HDL) potentially limits the oxidative modification of LDL by an enzymatic mechanism .The central role of paraoxonase (PON) 1 mechanism in the antioxidative actions of HDL by hydrolyzing LDL and cell membrane associated lipid hydroperoxides is well established ***(Mackness and Durrington, 1995).*** A greater degree of severity of the metabolic syndrome (MS) is associated with a progressively worse antioxidant/oxidant balance, and lower antioxidant PON1 enzymatic capacity ***(Sentí et al., 2003).***

Taurine (2-amino ethane sulphonic acid) is a derived amino acid that is found in high concentrations in most types of animal tissues ***(Nandhini et al., 2002b).*** The benefits of taurine supplementation have been reviewed with respect to diabetes, cardiomyopathy and hypertension. Specific hypolipidemc effects include increased activity of cholesterol 7 α-hydroxylase, increased LDL receptor binding, and increased LDL turn over ***(Militante and Lombardini, 2004).*** Previous studies have shown that taurine reduces oxidative stress in liver of high fructose fed rats ***(Nandhini et al., 2005a).***

Homocysteine (Hcy) is a derived sulfer-containing amino acid and an intermediary metabolic product derived from the demethylated essential amino acid methionine. The important role of oxidative-redox stress and hyperhomocysteinemia (HHcy) is biologically plausible because Hcy promotes oxidant injury to vascular cells through the auto-oxidation of Hcy, formation of mixed disulphides, interaction of Hcy thiolactones (HcyT), and protein homocysteinylation ***(Blom, 2000).***

It has been proposed that plasma Hcy levels are elevated in patients with chronic heart failure and may represent a new risk factor or risk marker for this condition. It has also been reported that blood Hcy levels are associated with the severity of the disease ***(Osorio et al., 2008).*** The oxidative stress accompanying this condition impairs insulin signaling and action therefore leading to IR ***(Najib and Sanchez-Margalet, 2001),*** and contributes to the associated vascular risk ***(Oron-Herman et al., 2005a).***

Previous reports show that insulin exerts desirable actions on the vasculature primarily by amplifying endothelium-dependant