



**Faculty of Science
Department of Zoology**

**Studying the Potential Palliative Activity of Selenium and Sulfur
Against Aluminum-Induced Toxicity in Adult Male Albino Rats**

A Thesis

**“Submitted as a Partial fulfillment for the requirements of Master
in Science”**

Naglaa Hussein Mohamed Nour-Eldein

Chemist at the Egyptian Mineral Resources Authority-Petroleum
Ministry
B.Sc., 2009

Under supervision of

Dr.Wael Mohamed El-Sayed

Professor of Physiology
Department of Zoology-Faculty of Science
Ain Shams University

Dr.El-Sayed Abdel-Khalik Hassanin

Head of Biochemistry and Nutritional Metabolism Department
National Institute of Nutrition
Ministry of Health
2017

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا

إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ (32)

صدق الله العظيم

(سورة البقرة)

Dedication

To my Parents,

To my brothers,

To my husband,

To my Son,

Zein

To Dr.Saed Soliman,

To Ahmed Hammad,

To Dr.Nermin,

And

To Yasmin Hosny Hassan

ACKNOWLEDGEMENTS

I am really indebted to my supervisor **Dr.Wael M. El-Sayed**, Professor of Physiology, Department of Zoology, Faculty of Science, Ain Shams University, Egypt for giving me the opportunity to perform this work under good working atmosphere, his encouragement, patience and interest that he showed in my work during the study period. I found him a true academician and I will always remember him with respect.

Thanks to **Dr. El-Sayed Abdel-Khalik Hassanin**, Head of Biochemistry and Nutritional Metabolism Department, National Institute of Nutrition, Ministry of Health for his assistance during this study.

Thanks to and Egyptian Mineral Resources Authority-Petroleum Ministry.

Thanks are also extended to head and members of Zoology Department, Faculty of Science, Ain Shams University

Contents

	Page
List of Abbreviations.....	i
List of Tables.....	iii
List of Figures	iv
Abstract.....	1
1. Introduction.....	3
Aim of Work.....	4
2. Review of literature.....	6
2.1. Aluminum	6
2.1.1. Toxicity.....	6
2.1.2. Absorption	7
2.1.3. Metabolism and Excretion.....	8
2.1.4. Mechanism of action.....	10
2.1.5. Effect of aluminum on liver function tests	10
2.1.6. Effect of aluminum on kidneys function tests	11
2.1.7. Effect of aluminum on lipid profile	11
2.1.8. Effect of aluminum on antioxidants	12
2.2. Selenium.....	12
2.2.1. Selenium forms	13
2.2.2. Sodium selenite chemical structure	14
2.2.3. Selenium exposure.....	15
2.2.4. Selenium protective action	16
2.2.5. Effect of sodium selenite on liver function tests	17
2.2.6. Effect of sodium selenite on kidney function tests.....	18
2.2.7. Effect of sodium selenite on Lipid profile.....	19

Contents (*cont....*)

2.2.8. Effect of sodium selenite on antioxidants.....	20
2.3. N-Acetylcysteine (NAC).....	21
2.3.1. Basic Pharmacology of NAC.....	22
2.3.2. Effect of NAC on liver functions.....	23
2.3.3. Effect of NAC on kidney functions	24
2.3.4. Effect of NAC on lipid profile.....	24
2.3.5. Effect of NAC on antioxidants	24
 3. Materials and Methods	 28
3.1. Animals and Experimental Design	28
3.1.1. Animals.....	28
3.1.2. Materials and chemicals	28
3.1.3. Experimental Design	29
3.2. Blood sampling	31
3.3. Tissue sampling and extraction.....	31
3.4. Biochemical Parameters.....	32
3.4.1. Determination of the activity (U/L) of alanine aminotransferase (ALT) in serum.....	32
3.4.2. Determination of the concentration (g/dl) of total protein .	32
3.4.3. Determination of concentration (g/dl) of albumin in serum.....	33
3.4.4. Determination of concentration (mg/dl) of creatinine in serum.....	34
3.4.5. Determination of gamma-glutamyl transpeptidase (γ -GT) activity (U/L) in serum	34
3.4.6. Determination of the concentration (mg/dl) of triacylglycerols (TAGs) in serum	35

Contents (cont....)

3.4.7. Determination of total cholesterol in serum (mg/dl)	36
3.4.8. Determination of high density lipoprotein cholesterol (HDL-cholesterol) in serum (mg/dl).....	37
3.5. Oxidative stress and antioxidants.....	38
3.5.1. Determination of lipid peroxide (Malondialdehyde; MDA) level in liver (μ moles/g tissue)	38
3.5.2. Determination of the reduced glutathione (GSH) level in liver (mg/g tissue)	39
3.5.3. Determination of vitamin E (μ g/ml) in serum.....	40
3.5.4. Determination of the catalase (CAT) activity (mmoles/g tissue) in liver.....	41
3.5.5. Determination of the activity (U/g tissue) of glutathione peroxidase (GPx) in liver	43
3.5.6. Determination of the activity (U/min/g tissue) of superoxide dismutase (SOD) in liver	44
3.5.7. Determination of the activity (mmoles/min/g tissue) of glutathione S-transferase (GST) in liver.....	46
3.6. In vitro assays.....	47
3.6.1. Peroxide scavenging activity	47
3.6.2. Superoxide anion scavenging activity	48
3.6.3. Free radical scavenging activity	48
3.6.4. Determination of the total antioxidant Capacity.....	49
3.7. Statistical analysis	49
3.8. Hitological methods	50
4. Results	51
5. Discussion	106
Summary	123
Conclusion	125

Contents (*cont....*)

References.....	127
Arabic Summary.....	
Arabic Abstract.....	

List of Abbreviations

Abbrev.	Full-term
4-AAP	4-Aminoantipyrine
Al ³⁺	Aluminum
AlCl ₃	Aluminum chloride
ALT	Alanine aminotransferase
APAP	Acetaminophen
ASC	Alanine-serine-cysteine
BCG	Bromo cresol green
CAT	Catalase
CDNB	1-Choloro-2,4-dinitrobenzene
CE	Cholesterol esterase
CHOD	Cholesterol oxidase
CYP7A1	Cholesterol7alpha-hydroxylase
DHBD	3,5-Dichloro2-hydroxybenzene sulfonic acid
DMSO	Dimethyl sulfoxide
DPPH	2,2 Diphenyl-1-picryhydrazyl
DTNB	5,5' Dithiobis2-nitro benzoic acid
FDA	Food and drug administration
GI	Gastrointestinal tract
GK	Glycerol kinase
GPO	Glycerol phosphate oxidase
GPx	Glutathione peroxidase
GR	Glutathione reductase
GS	glutathione-synthase
GSH	Reduced glutathione
GSSG	Disulfide form of glutathione
GST	Glutathione s-transferase
HDL-chol.	High density lipoprotein cholesterol
HIV	Human immunodeficiency virus
[•] OH	Hydroxyl radical
i.p.	Intraperitoneal
Ig E	Immunoglobulin E
Ig G4	Immunoglobulin G4
IL-4	Interleukin4

List of Abbreviations (*cont.....*)

Abbrev.	Full-term
INH	Isoniazid
iNOS	Nitric oxide synthase
LDH	Lactate dehydrogenase
LDL-chol.	Low density lipoprotein cholesterol
LPL	Lipoprotein lipase
LPO	Lipid peroxidation
LXR	Liver X receptor
MDA	Malonialdehyde
MPO	Myeloperoxidase
NAC	N-acetylcysteine
NADH	Reduced nicotinamide adenine dinucleotide
NADPH	Nicotinamide adenine dinucleotide phosphate
NBT	Nitro blue tetrazolium
NF-KB	Nuclear factor kappa-light-chain- enhance of activated B cells
O ₂ ^{•-}	Superoxide radical
PMS	Phenazine methosulfate
RER	Rough endoplasmic reticulum
ROS	Reactive oxygen species
SH	Sulfhydryl group
SHP	Small heterodimer partner
SOD	Superoxide dismutase
SS	Sodium selenite
T _{1/2}	Multiple half lives
TAGs	Triacylglycerols
TBA	Thiobarbituric acid
TBARS	Thiobarbituric acid reactive substances
TCA	Trichloroacetic acid
TEM	Transmission electron microscope
VLDL-chol.	Very low density lipoprotein cholesterol
WHO	World health organization
γ-GT	Gamma-glutamyl transpeptidase

List of Tables

Table No.	Title	Page
4.1	Effect of N-acetylcysteine and sodium selenite on body weight change % in rats.	51
4.2	Effect of N-acetylcysteine and sodium selenite on relative weight % of kidneys, liver and spleen in rats.	53
4.3	Effect of N-acetylcysteine and sodium selenite on serum alanine aminotransferase (ALT) activity, levels of total protein, albumin, globulins and A/G ratio in rats.	59
4.4	Effect of N-acetylcysteine and sodium selenite on serum creatinine level and gamma-glutamyl transpeptidase (γ -GT) activity in rats.	66
4.5	Effect of N-acetylcysteine and sodium selenite on serum levels of triacylglycerols (TAGs), total cholesterol (T.chol.), high density lipoprotein (HDL-chol.), low density lipoprotein (LDL-chol.), very low density lipoprotein (VLDL-chol.) and atherogenic indices in rats.	72
4.6	Effect of N-acetylcysteine and sodium selenite on the levels of malondialdehyde (MDA), reduced glutathione, (GSH) in liver and vitamin E in serum of rats.	82
4.7	Effect of N-acetylcysteine and sodium selenite on the activities of catalase, glutathione peroxidase (GPx), superoxide dismutase (SOD) and glutathione S-transferase (GST) in liver of rats.	88

List of Figures

Figure No.	Title	Page
2.1	Sodium selenite chemical structure	14
2.2	N-acetylcysteine (NAC) chemical structure	21
4.1	Effect of N-acetylcysteine and sodium selenite on body weight change % in rats	52
4.2a	Effect of N-acetylcysteine and sodium selenite on relative weight % of kidneys	54
4.2b	Effect of N-acetylcysteine and sodium selenite on relative weight % of liver	55
4.2c	Effect of N-acetylcysteine and sodium selenite on relative weight % of spleen	56
4.3a	Effect of N-acetylcysteine and sodium selenite on serum ALT activity (U/L) in rats	60
4.3b	Effect of N-acetylcysteine and sodium selenite on serum total protein level (g/dl) in rats	61
4.3c	Effect of N-acetylcysteine and sodium selenite on serum albumin level (g/dl) in rats	62
4.3d	Effect of N-acetylcysteine and sodium selenite on serum globulins level (g/dl) in rats	63
4.3e	Effect of N-acetylcysteine and sodium selenite on A/G ratio in rats	64
4.4a	Effect of N-acetylcysteine and sodium selenite on serum creatinine level (mg/dl) in rats	67
4.4b	Effect of N-acetylcysteine and sodium selenite on serum γ -GT activity (U/L) in rats	68
4.5a	Effect of N-acetylcysteine and sodium selenite on TAGs level (mg/dl) in rats	73
4.5b	Effect of N-acetylcysteine and sodium selenite on T.chol. level (mg/dl) in rats	74
4.5c	Effect of N-acetylcysteine and sodium selenite on HDL-chol. level (mg/dl) in rats	75
4.5d	Effect of N-acetylcysteine and sodium selenite on serum LDL-chol. level (mg/dl) in rats	76