Therapeutic impact of Grape (*Vitis vinifera*) leaves Polyphenols on neurological biomarkers of Alzheimer's dementia in aged rats

A Thesis Submitted for the degree of Ph.D. of Science in Biochemistry

By

Ghadha Ibrahim Fouad Abd El Aziz

Bachelor Degree (B.Sc.) in Science
(2005)
Master Degree (M.Sc.) in Science
(2014)

To
Biochemistry Department
Faculty of Science
Ain Shams University

2018

Therapeutic impact of Grape (*Vitis vinifera*) leaves Polyphenols on neurological biomarkers of Alzheimer's dementia in aged rats

A Thesis submitted for the degree of Ph.D. of Science in Biochemistry

By

Ghadha Ibrahim Fouad Abd El Aziz
Bachelor Degree (B.Sc.) in Science (2005)
Master Degree (M.Sc.) in Science (2014)

Supervisors

Prof. Dr. Ibrahim Hassan Borai
Professor of Biochemistry
Biochemistry Department
Faculty of science
Ain Shams University

Prof. Dr. Magda Kamal El-Din Ezz
Professor of Biochemistry
Biochemistry Department
Faculty of science
Ain Shams University

Prof. Dr. Maha Zaki Rizk
Professor of Biochemistry
Therapeutic Chemistry
Pharmaceutical and Drug Industries research division
National Research Center

Prof. Dr. Mahmoud El-Sherbiny Ramadan
Professor of Biochemistry
Therapeutic Chemistry
Pharmaceutical and Drug Industries research division
National Research Center

2018

Approval sheet

Title of thesis:

Therapeutic impact of Grape (*Vitis vinifera*) leaves Polyphenols on neurological biomarkers of Alzheimer's dementia in aged rats

Degree: Ph.D. of Science in Biochemistry

Name: Ghadha Ibrahim Fouad Abd El Aziz

This thesis for Ph.D. of Science Degree has been approved by:

This thesis has not been previously submitted for any degree at this or at any other university.

Signed,

Ghadha Ibrahim Fouad
2018

بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ

سورة يوسف

آية (76)

Dedication

This dissertation is lovingly dedicated to my *Mother*, who supported me each step through the duration of my studies, her support, encouragement, and endless love have sustained me throughout my life & to my *sister* Heba who had never left my side and she is very special.

I lovingly dedicate this thesis to my family, I love you.

Thank you,

Ghadha

Acknowledgement

To the almighty, most gracious and most merciful ALLAH, to him above all, humbly, apart from the efforts of myself, the success of any project depends largely on the encouragement and guidelines of many others. I take this opportunity to express my gratitude to the people who have been instrumental in the successful completion of this thesis.

A special gratitude I give to **Prof. Dr. Ibrahim H. Borai** and **Prof. Dr. Magda K. Ezz** whose contribution in stimulating suggestions and encouragement, supervision, in addition to, reading and criticizing the manuscript helped me to coordinate my research through the learning process of this Ph.D. thesis.

I would like to thank **Prof. Dr. Maha Z. Rizk**, for support, guidance, and supervision, as well as, the rest of my thesis committee including; **Prof. Dr. Hanan F. Ali, Prof. Dr. Mahmoud El-Sherbiny** and **Prof. Dr. Azza A. Matloub**. Furthermore, I would like to thank **Prof. Dr. Olfat Hammam**, Professor of Pathology at Theodor Bilharz Research Institute, for the histopathological study. Moreover, I would like to thank **Prof. Dr. Dalia Osama**, at Department of Pharmacology for her assistance in behavioural investigation.

Ghadha Ibrahim Fouad
2018

Contents

List of Abbreviations	I
List of Figures	V
List of Tables	VII
Abstract	1
1-Introduction	3
2-Aim of the work	6
3-Review of Literature	7
3.1. Ageing and Neurocognitive Decline.....	7
3.1.1. The brain	8
3.1.2. Neurodegenerative disorders.....	9
3.1.3. Dementia	11
3.2. Alzheimer's disease (AD) Etiology	13
3.2.1. Types of AD.....	13
3.2.2. Symptoms and stages of AD	14
3.2.3. Neuropathological hallmarks of AD	16
3.2.4. Biochemical processes related to underlying AD pathology….....	17
3.2.5. AD-associated Brain Changes	23
3.2.5.1. Neurotransmitters and Cholinergic Dysfunction	24
3.2.5.2. Neuroinflammation, neuronal and microvascular injury	26
3.2.5.3. Brain-derived neurotrophic factor (BDNF)	29
3.2.5.4. Oxidative stress and modified biology of ageing.....	31
3.3. Brain lipid homeostasis.....	34
3.3.1. Role of Cholesterol (metabolism, transport) and Homocysteine (HCy) in AD pathogenesis.....	35
3.3.2. Role of phospholipids and sphingolipids in amyloidogenesis.....	37