APPLICATION OF NANOTECHNOLOGY IN NATURAL COMPOUNDS FOR ANTIOXIDANT AND ANTICANCER PREPARATIONS

By

SAMAR ABD ELRAHEEM AHMAD ALI SHAHIN

B.Sc. Agric. Sci. (Biotechnology), Fac. Agric., Cairo Univ., 2007

THESIS

Submitted in Partial Fulfillment of the Requirements for the Degree of

MASTER OF SCIENCE

In

Agricultural Sciences

(Agricultural Biochemistry)

Department of Agricultural Biochemistry
Faculty of Agriculture
Cairo University
EGYPT

2019

Format Reviewer **Vice Dean of Graduate Studies**

APPROVAL SHEET

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SUPERVISION SHEET

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Title of Thesis: Application of Nanotechnology in Natural Compounds for Antioxidant and Anticancer Preparations
Supervisors: Dr. Ahmed Mahmoud Aboul-Enein
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Date: 28 /8 /2019

ABSTRACT

As multi-targeted compound, Thymoquinone (TQ) has been showed numerous therapeutic potentials in different diseases including cancers. Piperine has a wide range of pharmacological properties. It is used as an antioxidant, anti-cancer, etc, still not yet reach clinical use. This because some inherit limitations, as low bioavailability and solubility, targeting delivery, and selectivity. Here, in present studies have successfully tailored novel nanoformulations for TQ delivery relay on mesoporous silica nanoparticles (MSNs) as nanocarrier, and for Pip delivery relay on hydroxyapatite (HAP) as nanocarrier and made modification by adding phosphonate group (HAP-H) .TQ loaded into mesoporous of MSNs as core (MSNTQ), subsequently step, coating of the core with mixture of two different polymers-based designs to obtain shell layer (MSNTQ-WA, Whey protein-Arabic gum, and MSNTQ-CS, Chitosan-Stearic acid). The anticancer efficiency and selectivity in brain cancer cells (SW1088 and A172) compared to brain normal ones (HCN2) were investigated. The anticancer efficiency and selectivity of (HAP-Pip, HAP-H-Pip and Pip) in breast cancer cells (MCF7), colon cancer cells (CaCo2) and normal lungs (WI38) cell were used as normal cells. Furthermore . The results demonstrated that anticancer activity in term of cell viability was varied and found to be cell line- With respect of biocompatibility of nanocarrier, and less toxic on normal than cancer cells Going further, the selective index calculations based on IC_{50} values verified that MSNTQ-WA, HAP-H-Pip exhibited better selectivity compared to all. Collectively, as the molecular mechanisms of action are concerned, the important findings is that nanoformulations especially MSNTQ-WA allowed remarkable effect to improve caspase-3 activation, Cytochrom c triggers, cell cycle arrest at G2/M phase and HAP-H-Pip has apoptosis induction compared to Pi in brain cancer cells.

Keywords: Cancer selectivity, Drug delivery systems, Thymoquinone nanoformulations, Mesoporous silica nanoparticles, Brain cancers. Piperine nanoformulations, Hydroxyapatite nanoparticles, Breast and colon cancer.

DEDICATION

*I dedicate this work to whom my heartfelt ,to my late **father** and my beloved queen **mother** whose taught me how to fight with honor till I reach my goal;my (**brother** and **sisters**) whose encouraged me when I fall down ; my small family (**Husband** and **Son**) for all the support they lovely offered along the period of my post-graduation; **Mohammad Ebrahim,Amr Abou-Elhamad and Elshaimaa Ahmad** whose supported me a lotto continueandfinally **my colleagues** whom help, support me a lot and encouraged me when I faint ; and your support made me able to gain such success and honor.*

Thanks from the earth to the edge of the universe.

ACKNOWLEDGMENTS

First, I would like to express my great thanks to Allah, for giving me the patience and the power to overcome all problems, which faced me throughout this work.

I would like to express my greatest appreciation, deepest thanks to my supervisor ***Dr. Ahmed Aboul-Enein****, Prof.of Biochemistry,Faculty of Agriculture, Cairo University for his encouragement and his beneficial criticism, indispensible advice, helpful, suggestions, his valuable supervision and valuable time devoted during the preparation of this thesis.*

I am profoundly grateful to ***Dr. Faten Aboul-Ela,*** *Prof. of Biochemistry, Faculty of Agriculture, Cairo University for her kind supervision, continuous encouragement, comments and the time she freely gave me during this work.*

I would like to express my great indebtedness, deepest thanks and sincere gratitude to my supervisor ***Dr.Khaled Abou-Eitta****, Researcher,Medicinal and Aromatic Plants Research Department,National Research Center, for suggesting the subject her valuable supervision constant beneficial criticism indispensible advice, generous help, and supplying all the facilities throughout the whole time of this work.*

I wish to express my indebtedness and profound gratitude to ***Dr. Abdalla M .A. Abdullah,*** *Professor of Agricultural biometry agronomy department faculty of Agriculture, Cairo University. For statistical analysis to the obtained data.*

I wish to express my indebtedness and profound gratitude to ***Dr.Esam R. Ahmed****, Confirmatory Diagnostic Unit, (VACSERA), Giza,Egypt.*

LIST OF ABBREVIATIONS

API=Active Pharmaceutical Ingredient.
BBB=the blood-brain barrier.
BET=Brunauer-Emmett-Teller.
CAT=catalase.
CTAB= Cetyltrimethylammonium bromide.
CS= Chitosan.
DDSs= Drug delivery systems.
Dime DFT= Density functional theory.
Dimethylsulfoxide = DMSO.
DOX=Anticancer drug doxorubicin.
DPPH=(2,2-diphenyl-1-picrylhydrazyl).
DSC=Differential Scanning Calorimetry.
2D-NMR=Two-dimensional nuclear magnetic resonance.
3D=Three dimensional.
EDC=1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride.
EGCG=Epigallocatechin- 3-gallate.
ERK =extracellular-signal-regulated kinase.
FA=Folic acid.
FACS=Fluorescence-activated cell sorting.
FTIR=Fourier transform infrared spectroscopy.
Fourier Transform Infrared spectroscopy.
GPx=glutathione peroxidase.
GRed= glutathione reductase
HAP=Hydroxyapatite Nanoparticles**.**
HR-TEM=High resolution transmission electron microscopy.
HPLC= High Performance Liquid Chromatography.
HP=Hydroxyapatite .
HSNPs=Hollow silica nanoparticles.
KCC-1=Fibrous silica nanospheres introduced by KAUST Catalysis Center.
MCM-41=Mobil Composition of Matter No. 41 mesoporous silica material.
MMP9=Matrix metallopeptidase 9.
MSNs=Mesoporous silica nanoparticles.

MSNTQ-CS= Mesoporous silica nanoparticles thymoquinone-chitosan-stearic acid .
MSNTQ-WA= Mesoporous silica nanoparticles thymoquinone-Whey protein-Arabic gum.
MTX=Methotrexate.
NF-κB=Nuclear factor kappa-light-chain-enhancer of activated B cells.
PBS=Phosphate buffer saline.
PCS=photon correlation spectroscopy.
PI3K/AKT=Phosphatidylinositol-3-kinases/AKT pathway
PIP= Piperine.
PKC= Protein kinase C.
PLGA = Poly(D, L-lactide-co-glycolide
Prx=peroxiredoxin
PPAR-=Peroxisome proliferator-activated receptor gamma.
PTA-CS-MNP=phytic acid-chitosan-iron oxide nanocomposite.
PXRD=powder X-ray diffraction.
SEM=Filed emission scanning electron microscopy.
SLN=Solid lipid nanoparticle.
SOD=Superoxide dismutase
STA-FTIR=Simultaneous Thermal Analysis coupled with
TBAR= Tthio-barbituric acid-reactive.
TEA=Triethanolamine
TEM=transmission electron microscopy.
TEOS=Tetraethyl orthosilicate.
TGA=Thermogravimetric analysis.
TLC=Thin Layer Chromatography.
TQ=Thymoquinone.
WHO=World Health Organization.
XIAP= X-linked inhibitor apoptosis protein.
XRD=X-Ray diffraction.

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