Evaluation of antitumor activity of nanogallium and low dose of gamma irradiation in animal model

A Thesis
Submitted to Faculty of Science, Ain Shams University
For Partial Fulfillment of
Master degree of Science
in Biochemistry

By

Ola Mohamed Sayed Khedr
B.Sc. in Biochemistry and Chemistry (2011)

Faculty of Science
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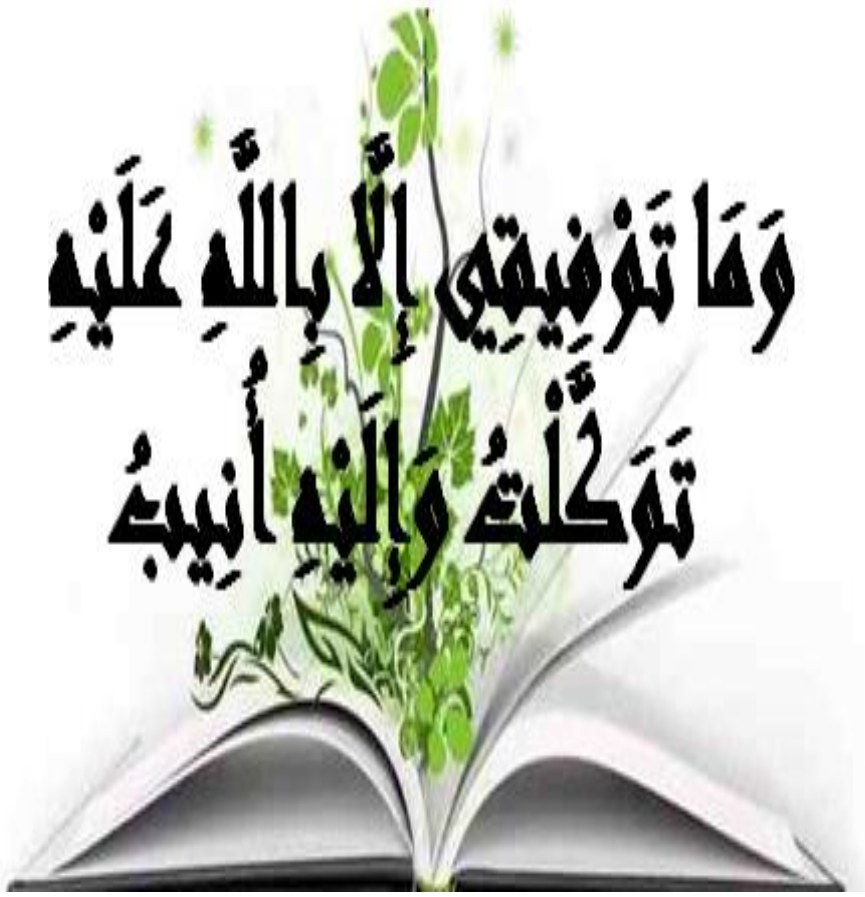
2017

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ



وَمَا تَوْفِيقِي إِلَّا بِاللَّهِ عَلَيْهِ
تَوَكَّلْتُ وَإِلَيْهِ أُنِيبُ

Approval Sheet

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Submitted to

Biochemistry department, Faculty of Science, Ain Shams University

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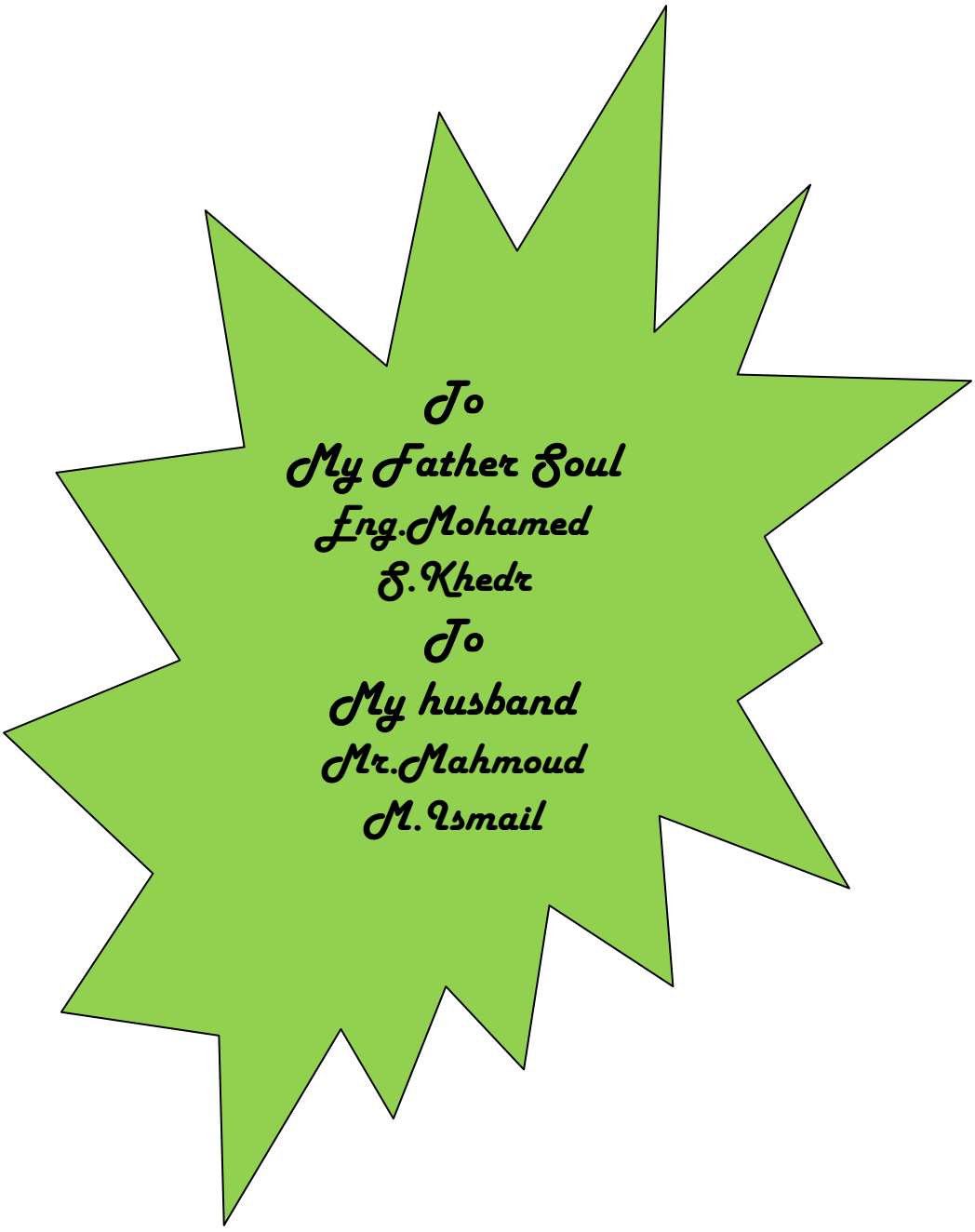
First, foremost, and all thanks to Allah by whose grace this work had been completed and by whose grace all my life is arranged in the best. Nobody can imagine this way that had been drawn by the mercifulness of Allah.

Declaration

I declare that this thesis has been composed by me and it has not been submitted for a degree at this or any other university.

Ola Mohamed Sayed Khedr


To
My Father Soul
Eng.Mohamed
S.Khedr
To
My husband
Mr.Mahmoud
M.Ismail

Dedication

I dedicate this work to all members of my dear family for their support and continuous backing in which this work was accomplished.

Ola Mohamed Sayed Khedr

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Abstract

ABSTRACT

Chemotherapy combined with radiotherapy is approach for cancer treatment. In the present study, Gallium nanoparticles were biologically synthesized by using *Lactobacillus helveticus* extracellular metabolites. Gallium nanoparticles were characterized by using transmission electron microscopy (TEM) analysis, Fourier transforms infrared spectroscopy (FTIR) and Ultraviolet-visible absorption (UV/VIS), revealed that; GaNPs were of size ranging 6–20 nm. The FTIR analysis of GaNPs showed shifting in wave number of functional groups due to their involvement in GaNPs capping and synthesis. UV/VIS scan showed absorption peak of GaNPs at 265 nm. GaNPs effectively inhibited MCF-7 proliferation *in vitro* with IC_{50} of 8.0µg/ml. *In vivo* study, GaNPs LD_{50} was found to be 10 mg/kg b.w. Evaluation of GaNPs antitumor effect and/or gamma radiation *in vivo*, was performed using 80 female swiss albino mice. They were divided into 8 groups, each of 10 mice. Mice were inoculated intramuscular with Ehrlich ascite carcinoma cells in the right thigh to induce a solid tumor. The results revealed that solid tumor induced a significant increase in serum ALT activity, serum creatinine level, total leucocytic count, liver MDA content, liver calcium and liver iron concentrations While GSH, CYP2E1 and Na^+K^+ATPase showed significant decrease compared to control group.Treating Ehrlich carcinoma (EC) bearing mice with GaNPs and/or exposure to low dose of γ-radiation (0.25 Gy) significantly reduced tumor volume, ALT activity, creatinine level and TLC in mice serum and blood respectively. Moreover, biochemical studies in the liver tissue showed a significant increase in glutathione level, Na^+K^+ATPase activity, CYP450 (2E1) gene expression with a significant decrease in MDA content, the calcium and iron concentrations compared to EC group. Meanwhile, biochemical studies in the tumor tissue showed a significant increase in MDA content, Na^+K^+ATPase, complexes II and III activity with a significant reduction in GSH level, calcium, iron concentrations and CYP450 (2E1) gene expression in mitochondria upon comparison with EC group. Also DNA fragmentation pattern of tumor tissue showed intense fragmentation accompanied with different treatments compared to EC group. Results indicate a synergestic effect of combined treatment against Ehrlich solid tumor which was well confirmed with the histopathological findings in the tumor tissue of treated groups compared to EC group.

List of Abbreviations

ADP	Adenosine DiPhosphate
ALT	Alanine Aminotransfese
ANOVA	Analyzed Using One way analysis of Variance
AsGa	Arsenium–Gallium
ATCC	Addiction Technology Tranfer Centre
ATP	Adenosine TriPhosphate
BAX	Bcl-2-associated X protein
BREC	Bovine Retinal Endothelial Cells
C	Control
Ca	Calcium
CoQ	Coenzyme Q
Cs	Caesium
CYP P450	Cytochrome P450
CYP2E1	Cytochrome P450 2E1
Cyt c	cytochrome c
DMSO	Dimethyl sulfoxide
DNA	deoxyribonucleic acid
dNDP	desoxynucleotide diphosphate
DTT	Dithiothreitol
EAC	Ehrlich Ascites Carcinoma
EC	Ehrlich Carcinoma
EDTA	Ethylene Diamine Tetra Acetic Acid
ELISA	Enzyme-linked immunosorbent assay
EPR	Enhanced permeability and retention