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Potential Antitumorgenic Effect of Garlic (*Allium Sativum*) Oil in Female Mice Injected With Ehrlich Ascites Carcinoma Cells

Thesis

Submitted to Faculty of Women, Ain Shams University
In Partial Fulfillment for the Master of Science Degree (MSc) in Biochemistry and Nutrition

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2015

بسم الله الرحمن الرحيم

صدق الله العظيم

البقرة (32)

Acknowledgement

*First of all and foremost, thanks to **Allah** almighty for giving me the strength and the incentive to peruse this career and who allowed me to have the privilege of doing this work.*

*I would like to express my deepest most sincere appreciation and gratitude to **Dr. Gehan Salah Eldin Moram,** Assistant Professor of Nutrition, Biochemistry and Nutrition Department Faculty of Women for Arts, Science and Education, Ain Shams University, for her guidance, care and continuous supervision and encouragement; she has been a tremendous mentor for me.*

*I would also like to deeply thank **Dr. Nahla Hussein Ali,** Assistant Professor of Nutrition, Biochemistry and Nutrition Department, Faculty of Women for Arts, Science and Education, Ain Shams University, for the great help that she offered, and whose directions sat me on the right track, and made the completion of this work possible.*

*I would like to extend my thanks to **Dr. Hala Salah Abd El Fatah,** Lecturer at Biochemistry and Nutrition Department, Faculty of Women for Arts, Science and Education, Ain Shams University for her appreciable contributions to this work.*

*I am thankful to **Dr. Ola Nada,** Assistant professor of clinical pathology, Al Azhar University for the help that she offered in the histopathological examination carried out in this study.*

*Last but not least, infinite thanks to **My family** for their continuous encouragement, support and everything else...*

Ola Mohamed Samy

Abstract

Cancer is a multifactorial heterogeneous disease and identification and use of effective cancer chemopreventive agents is an important issue in public health-related research. Habitual use of functional foods such as garlic is examined in the battle against cancer and its eradication program The main goal of this study was to evaluate the antitumor and antioxidant potential of garlic oil (GO) in vivo using Ehrlich Ascites Carcinoma (EAC) cell line.

The results of GO analysis using GC-MS revealed that it contained 35.1% diallyl disulphide (DADS), 27.5% diallyl trisulphide (DATS), 17.5% diallyl sulphide (DAS), and varying amounts of many other sulfur containing compounds. The results of the animal trial illustrated that: The antitumor potential of GO was evident through the decrease in tumor weight and volume, the prolongation of the life span of tumor bearing mice (TBM) up to 53.57%, regression in tumor growth rate that reached 36.38 % and inhibition of histone deacetylase (HDAC) enzyme activity up to 9.4%, 14.4% and 18.4% in isolated peripheral blood mononuclear cells, liver and tumor tissues, respectively. EAC injection caused a severe oxidative stress in TBM compared to healthy mice. However, GO successfully elevated the depleted total antioxidant capacity (TAC) to near normal level. Also, reduced glutathione (GSH) was dramatically increased in GO administered mice with its level rising up to 66.3% compared to TBM. Catalase (CAT) and glutathione-S- transferase (GST) activities were both significantly elevated. The increments in CAT activity mounted up to 19.7%, 56% and 68% in serum of GO receiving groups; G4, G5, and G6 respectively, **P<0.05**. The activity of GST was increased by 12.9 %, 42.5 % and 63.8 % respectively at the same manner, **P<0.05**. GO reduced the marked elevation of malondialdehyde (MDA) concentration in GO receiving groups; G4, G5, and G6 to 4.85 ± 0.5 mmol/L, 4.29 ± 0.5 and 3.84 ± 0.34 mmol/L respectively, **P < 0.05**. Changes in oxidative stress markers measured in liver or tumor tissue homogenates mirrored those measured in blood. Concerning the hematological parameters, GO resulted in a significant reduction in the white blood cells (WBCs) count and elevation of hemoglobin (Hb) concentration as well as the red blood cells (RBCs) count. There were noticeable improvements in blood indices as well. GO resulted in an improved liver function represented by the decrement of liver enzymes' activities and the restoration of blood proteins levels. Histopathological examination of the liver confirmed the results of the biochemical analysis showing the hepatoprotective and antitumor effects of GO.

List of Abbreviations

5-HIAA	**5-Hydroxy Indole Acetic Acid**
5-HT	5-Hydroxy Tryptamine
5-LOX	5-Lipoxygenase
A/G ratio	Albumin/Globulin Ratio
AA	Ascorbic Acid
AAP	4-Aminophenazone
ACF	Aberrant Crypt Foci
AGE	Aged Garlic Extract
Ak_t	Mouse Thymoma Oncogene-Member of the protein kinase B-family
ALT	Alanine Aminotransferase
ANOVA	Analysis of Variance
AST	Aspartate Aminotransferase
ATP	Adonesine Triphosphate
Bcl-2	B-cell lymphoma 2
Bcl-xL	B-cell lymphoma- xL
CAM	Complementary and Alternative Medicine
CAT	Catalase
CCl_4	Carbon tetrachloride
CDNB	Chloro-2,4-dinitrobenzene
CEB	Cytosol Extraction Buffer
COX-2	Cyclooxygenase-2
CYP 450	Cytochrome P450
DADS	Diallyl Disulfide
DAS	Diallyl Sulfide
DATS	Diallyl Trisulfide
DHBS	3,5-Dichloro-2-HydroxyBenzene Sulfonic acid
DMBA	7, 12-DimethylBenzo[a]Anthracene
DMH	1,2- Dimethylhydrazine
DNA	Deoxyribonucleic Acid

DPPH	1,1-Diphenyl-2-Picryl-Hydrazyl
DTNB	5,5'-Dithiobis 2-Nitrobenzoic acid
DTT	Dithiothreitol
EAC	Ehrlich Ascites Carcinoma
EDTA	Ethylene Diamine Tetracetic Acid
EGFR	Epidermal Growth Factor Receptor
ELISA	Enzyme Linked Immunosorbent Assay
EMEA	European Medicines Evaluation Agency
ESC	Ehrlich Solid Carcinoma
FDA	Food and Drug Administration
Fe- NTA	Ferric Nitrilotri Acetate
GC- MS	Gas Chromatography- Mass Spectrometry
GO	Garlic Oil
GO pr	Garlic oil protection
GO Pr+ Tr	Garlic oil protection + treatment
GO Tr	Garlic oil treatment
GR	Glutathione Reductase
GSH	Reduced Glutathione
GSH-Px	Glutathione Peroxidase
GSSG	Glutathione Disulfide (oxidized)
GST	Glutathione-S transferase
HAT	Histone acetyl transferase
Hb	Hemoglobin
HCT	Hematocrit
HDACIs	Histone Deacetylase Inhibitors
HDACs	Histone Dacetylases
HER2	Human Epidermal growth factor Receptor 2
HRP	Hydrogen Peroxidase
IKK	Ikappab Kinase
IL	Interleukin
ILS %	Increased Lifespan %

IM	Intramuscular
JNK	Jun N-Terminal Kinase
LDL-C	Low Density Lipoprotein Cholesterol
MAPK	Mitogen-Activated Protein Kinase
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
MDA	Malondialdehyde
MNU	N-methyl- N-Nitroso Urea
MST	Mean Survival Time
MTW	Mean Tumor Weight
NAD	Nicotinamide Adenine Dinucleotide
NCI	National Cancer Institute
NDEA	Nitrosodiethylamine
NF-kB	Nuclear Factor-kappa B
NTBM	Non- Tumor Bearing Mice
OD	Optical Density
OSCs	Organosulphur Compounds
PARP	Poly (ADP-Ribose) Polymerase
PBMC	Peripheral Blood Mononuclear Cells
PBS	Phosphate Buffer Saline
PTI	Post tumor inoculation
RBCs	Red Blood Cells
RNA	Ribonucleic Acid
ROS	Reactive Oxygen Species
Rpm	Round Per Minute
RT-PCR	Real-Time –Polymerase Chain Reaction
SAC	S-Allylcysteine
SAMC	S-Allylmercaptocysteine
SOD	Superoxide Dismutase
SPSS	Statistical Package for Social Science
STAT3	Signal Transducer and Activator of

	Transcription 3
T/G %	Tumor Growth Inhibition Ratio
TAC	Total Antioxidant Capacity
TBA	Thiobarbituric Acid
TBM	Tumor Bearing Mice
TCA	Trichloroacetic Acid
Th1	T-helper-Type 1 cells
Th2	T-helper-Type 2 cells
TRP	Tryptophan
WBCs	White Blood Cells

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