# MODULATION OF RADIATION BIOHAZARDS USING A COMBINATION OF SILYMARIN, VITAMIN E AND SELENIUM IN EGYPTIAN URANIUM MINERS

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*M.B.B.Ch, Ain Shams University (١٩٨٥)*

*M.Sc., in Pediatric Medicine, Ain Shams University (١٩٩٤)*

***A Thesis Submitted in Partial Fulfillment of***
***The Requirement for the Doctor of Philosophy***
***In Environmental Science***

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**Institute of Environmental Studies and Research**

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# Acknowledgement

*I am deeply indepted to* ***Prof. Dr Nabil Abd Ulkader Saleh****, Professor of Biochemistry, Faculty of Science, Ain Shams University for his suggesting the problem, his close supervision, and wise advise that helped me too much in this work .*

*I would like to express my sincere gratitude* ***Prof. Dr Ahmed Esmat Shoman,*** *Professor of Occupationally and Environmental-Community, Faculty of Medicine, Ain Shams University, for his patience, his meticulous observation and continuous encouragement.*

*I wish also to express my deepest gratitude to* ***Prof. Dr. Mahmoud Hani Shalaby,*** *Professor of Geology, Nuclear Material Authority for his valuable advise, support, and for his great help in the geological part of this work*

*I wish to express my deepest thanks to* ***Prof. Dr. Said Salama Moselhy,*** *Professor of Biochemistry, Faculty of Science, Ain Shams University, for his guidance, valuable help, kind directions and generous support during the practical part of this study.*

*I wish also to express my deepest thanks to* ***Dr. Mohamed Farag Hammad*** *the general manager of the Medical and Radiological Protection Department of Nuclear Material Authority for his help in the practical part of this work, beside his continuous encouragement and advice to end this work.*

*I would like to thank all the* ***Members of Gattar Regions*** *for their help and cooperation in the practical part of this work.*

*Also my sincerest thanks to* ***Dr. Nihad Ahmed Elnashar*** *Assistant Professor of Clinical Pathology, National Center for Research and Technology, Atomic Energy Commission of Egypt for her kind assistance in the statistical and practical part of this work.*

*Last but not least I own a great appreciation to* ***my colleagues*** *in Medical Department in the Nuclear Material authority, also* ***my close and big family*** *for their unfailing support and encouragement.*

***Dr. Manal Ahmed Elnashar***

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# ABBREVIATIONS

**μ SV/h:** ..... Microsevert per hour

**γ-rays** : ..... Gamma rays

**٠٣:** ..... Ozone .

**$O^{\cdot -}_{٢}$** ..... Singlet oxygen

**٦PGD:** ..... ٦ - phosphogluconate dehydrogenase.

**AC**: ..... Adenocarcinoma .

**ADR**: ..... Adriamycin

**ALARA** : ..... As Low As Reasonable Achievable .

**ALT&AST:** ..... Serum alanine and aspartate aminotransferase.

**ALP:** ..... Alkaline Phosphatase.

**AP-١ activation:** Activator protein-١:

**ATP:** ..... Adenosine triphosphate

**BSP:** ..... Biological Signal Processing.

**$Ca^{+٢}$:** ..... Calcium ion

**CAT:** ..... Catalase

**CD٤+ T cells:** ..... T cells Expressing CD٤.

**CDKs:** ..... Cyclin-dependent kinases

**CL**: ..... Chloride ions

**CoQ ١٠:** ..... Coenzyme Q١٠, ubiquinone

**CPD:** ..... Cyclobutane pyrimidine dimers

**CRP:** ..... C-reactive protein

**Cu:** ..... Copper

**CuZn.SOD:** ..... (Cupro-zinc) superoxide dismutase

**DNA:**..... Deoxy ribonucleic acid

**DPI:** ..... Diphenyliodonium .

**DTNB:** ..... Ellman s Reagent

**EASIA:** ..... Enzyme Amplified Sensitivity Immunoassay .

**EDTA:** ..... Ethylenediaminetetraacetic acid:

**EIA:** ..... Enzyme immunoassay.

**EPO:** ..... Erythropoitin

**ERKV٢**:..... Extra-cellular signal regulated protein kinase

**$Fe^{+٢}$:** ..... Ferrous ion

**$Fe^{+٣}$:** ..... Ferric ion

**G٦PD:**..... Glucose - ٦ - phosphate dehydrogenase .

**G-I:**..... Gattar-١

**G-II:** ..... Gattar-II

**GM-CSF:**.....Granulocyte macrophage colony stimulating factor

**GPX:**..... Glutathione peroxidases, Guaifenesin Phenylephrine

**GR:**..... Glutathione reductase.

**GSH:** ..... Reduced glutathione peroxidase

**GSHc:** ..... The concentration of GSH in the cuvette sample.

**GSSG:**..... Oxidized glutathione.

**Gy:** ..... Gray unit

**$H_٢O_٢$:** ..... Hydrogen peroxide.

**HCC:**..... Hepatocellular carcinoma.

**Hep٣B**:..... Hepatitis B virus positive; p٥٣ mutated

**HepG٢**: ..... Hepatitis B virus negative; p٥٣ intact.

**HIV-١:** ..... Human immunodeficiency virus

**$HNO_٢$:**..... Nitrous acid

**$HO^{\cdot ٢}$:** ..... Hydroperoxyl radical

**$HO_٢$:** .....Hydroperoxyl

**HOCL**: ..... Hydrogen hypochlorous acid.

**HRP:** ..... Horseradish peroxidase ()-labelled-antibody

**HUVECs:** ..... Human Umbilical Vein Endothelial Cells

**I.N.T:** ..... ٢-(٤-iodophenyl)-٣-(٤-nitrophenol)-٥-phenyltetrazolium chloride

**I١٣١:** ..... radioactive iodine isotope

**IFN-γ**:..... Interferon gamma

**IgA:**..... Immunoglobulin A

**IgG:** ..... Immunoglobulin G

**IgM:** ..... Immunoglobulin M

**IHD**: ..... International Healthcare Distributors:

**IKK:**..... I kappa B kinase.

**IL-٢**: ..... Interlrukin ٢

**IL-٢R:**..... Interleukin ٢ receptor

**IL-٢ mRNA** : ..... Interleukin -٢ messenger ribonucleic acid.

**IL-٤:** ..... Interleukin ٤

**IL-٦:** ..... Interlrukin ٦

**IL-٦R:**..... Interleukin ٦ receptor

**IL-٨:** ..... Interlrukin ٨

**IU/d:**..... International unit/day

**J٧٧٤.١ and RAW٢٦٤.٧ cells** : RAW٢٦٤.٧ and J٧٧٤.١ macrophage-like cell lines

**JNK١:** ..... C-Jun N-terminal kinase ١ **or** Stress-activated protein kinase ١

**KPA:** ..... Kinetic phosphorescence analyzer.

**LAK:**..... Lymphokine activated killer.

**LOOH**: ..... Lipid hydroperoxide .

**LPS:** ..... Lipopolysaccharide

**LT-α:** ..... Lymphotoxin-alpha

**LT-β:**..... Lymphotoxin-beta

**MAbs:** ..... Monoclonal antibodies .

**MAPK kinase activation:** Mitogen-activated protein kinase

**MCSF:** ..... Monocyte colony stimulating factor

**MDA:** ..... Malondialdehyde

**MEK:** ..... MAP kinase kinase:.

**MHC:**..... Major heart compatibility complex

**MNCs**:..... Mononuclear cell

**MnSOD**:..... Manganese superoxide dismutase

**mRNA**:..... Messenger ribonuclear acid

**MSeA:**..... Methylselenic acid

**$MS_V$:** ..... Milli severt

**NAC:** ..... N-acetly cysteine.

**NADH:**..... Nicotin amide adenine dinucleotide

**NADPH** : ..... Nicotinamide adenine dinucleotide phosphate.

**NFAT**: ..... Nuclear factor of activated T cells.

**NF-Bκ:**..... Nuclear factor-kappa light chain inhancer of activated B cell

**NF-kappa:** ..... Nuclear factor-kappa light chain inhancer of activated B cell

**NF-KB:** ..... Transcription factor nuclear factor

**NK:**..... Natural killer cell

**NMA:**..... Nuclear material authority

**$NO^{\bullet}$:** ..... Nitric oxide.

**NOS-٢:**..... Nitric oxide synthase-٢

**O.D.:** ..... Optical Density.

**$O^{\bullet ٢}$:** ..... Singlet oxygen .

**$O^{-٢}$:** ..... Superoxide .

**OFR** : ..... Oxygen free radicals .

**OH.:** ..... Hydroxyl

**PAO** : ..... Phenylarsine oxide .

**PBMCs**: ..... Prepherial blood mononuclear cells

**PCV:** ..... Packed cell volume .

**ρH:** ..... Degree of olkalinity or acidity

**PHA stim:**..... Phytohaem-agglutinin stimulator

**PKA:**..... Protein kinase-C-

**PUFA:** ..... Polyunsaturated fatty acids .

**RBCs**: ..... Red blood cells .

**RDA:** ..... The recommended daily allowance .

**$Rn^{٢٢٢}$:**..... Radon ٢٢٢

**RNA:**..... Ribonucleic acid

**RnDP:**..... Radon daughtu product

**RO:**..... Alkoyxl radical

**$RO_{٢}$**: ..... Peroxyl .

**$RO_{٦}$:**..... Peroxyl radical

**ROS:** ..... Reactive Oxygen Species

**S.VCAM-١:** ..... Soluble vascular cell adhesions molecule

**SCF:**..... Stem cell factor

**SCLC**: ..... Small cell lung carcinoma.

**Se** : ..... Selenium

**Se-GSH-Px :** ..... Selenium dependent glutathione peroxidase

**SOD:** ..... Superoxide dismutase .

**SqCC:** ..... Squamous cell carcinoma .

**$Sr^{٩٠}$:** ..... Strontium-٩٠.

**TACE** : ..... TNF-α converting enzyme .( for TNF see below)

**TAD:**..... Total annual dose

**TPR**:..... Transporter protein receptor

**TGFB:**..... Transforming growth factor B

**$Th_1$:** ..... T helper cell - ١

**$Th_2$:** ..... T.helper cell - ٢

**$Th^{231}$:** ..... Thorium ٢٣١

**TMG**: ..... Alpha-tocopherol monoglucoside

**TNF-α:**..... Tumor necrosis factor α

**TNF-β:**..... Tumour necrosis factor β

**TR:**..... Thioredoxin reductase .

**U/G**:..... Under ground

**$U^{238}$:** ..... Uranium ٢٣٨

**$U^{239}$:** ..... Uranium ٢٣٩

**$UF_6$:**..... Uranium hexafluoride .

**UNH:**..... Uranyl nitrate hexahydrate .

**UVA:** ..... Ultraviolet A

**VCAM-١:** ..... Vascular cell adhesion molecule-١ .

**Vit E.**: ..... Vitamin E radical ( a - chromanoxyl radical)

**WL:**..... Working level

**XOD:**..... Xanthine oxidase

**ά-particles**: ..... Alpha particles

**α-rays**: ..... Alpha rays

**β-rays**: ..... Beta rays

**γ-GT:**..... γ Glutamyl Transferase

**ABSTRACT**

The current study was carried out to evaluate the intensity of oxidative tissue damage induced by short and long exposure to ionizing radiation among Egyptian uranium miners as well as the displayable protective role of the triple antioxidants administration of Silymarin, Selenium and Vitamin E in such cases.

Fasting plasma malondialdehyde (MDA), erythrocyte superoxide dismutase (SOD) activity, blood reduced glutathione (GSH), serum interleukin – ٢ (IL-٢), serum IL-٦, serum TNF-α levels were determined pre and post triple antioxidants (TAC) administration of Silymarin, in a total daily dose of ٢١٠ mg divided into ٣ doses. (As Legalon ٧٠ mg three times /day). Selenium, ٢٠٠ -٣٠٠ µg per day (As selenium ١٠٠, One capsule twice a day) and Vitamin E, ٧٠ mg per day (As α-tocopherol, One capsule twice a day), for ١٢ months in ٢٠ uranium miners working ٢-٥ years (group II), ٢٠ uranium miners working ≥١٠ years (group III). In addition two further groups were taken from the working miners for the same period of exposure (IV, V) without administration of (TAC). The obtained results were statistically analyzed and compared to those obtained from ٢٠ non smoking healthy age and sex matched volunteers (group I) as control.

Regarding the groups (II, III), post - TAC administration It was found that, a significant decrease in plasma MDA, erythrocyte SOD activity, serum IL-٢, IL-٦ and TNF-α, while blood GSH was significantly elevated as compared to control group (group ١).

Our results ascertained the unique potential ameliorative role displayed by triple antioxidants administration of Silymarin, selenium and Vitamin E as free radical scavengers, against cellular damage induced by the ionizing radiation emitted from Uranium ٢٣٨ ($U^{٢٣٨}$) among Egyptian uranium miners.