

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

By

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

Department of Medical Science
Institute of Environmental Studies and Research
Ain Shams University

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ABBREVIATIONS

μ SV/h:		Microsevert per hour
γ -rays :		Gamma rays
O_3 :		Ozone .
$O^{\cdot-}$		Singlet oxygen
γ PGD:		γ - phosphogluconate dehydrogenase.
AC:		Adenocarcinoma .
ADR:		Adriamycin
ALARA :		As Low As Reasonable Achievable .
ALT&AST:		Serum alanine and aspartate aminotransferase.
ALP:		Alkaline Phosphatase.
AP-1 activation:		Activator protein-1:
ATP:		Adenosine triphosphate
BSP:		Biological Signal Processing.
Ca^{+2} :		Calcium ion
CAT:		Catalase
CD4+ T cells:		T cells Expressing CD4.
CDKs:		Cyclin-dependent kinases
CL:		Chloride ions
CoQ 10:		Coenzyme Q10, 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
ERKγ:	Extra-cellular signal regulated protein kinase
Fe^{+2}:	Ferrous ion
Fe^{+3}:	Ferric ion
GαPD:	Glucose - 6 - phosphate dehydrogenase .
G-I:	Gattar-I
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$_2$O$_2$:	Hydrogen peroxide.
HCC:	Hepatocellular carcinoma.
HepγB:	Hepatitis B virus positive; p $\alpha\gamma$ mutated
HepGγ:	Hepatitis B virus negative; p $\alpha\gamma$ intact.
HIV-1:	Human immunodeficiency virus
HNO$_2$:	Nitrous acid
HO$^{\gamma}$:	Hydroperoxyl radical
HO$_2$:	Hydroperoxyl

HOCL:		Hydrogen hypochlorous acid.
HRP:		Horseradish peroxidase ()-labelled-antibody
HUVECs:		Human Umbilical Vein Endothelial Cells
I.N.T:		γ -(ϵ -iodophenyl)- γ -(ϵ -nitrophenol)- α -phenyltetrazolium chloride
I^{125}:		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-γ:		Interlukin γ
IL-γR:		Interleukin γ receptor
IL-γ mRNA :		Interleukin - γ messenger ribonucleic acid.
IL-ϵ:		Interleukin ϵ
IL-δ:		Interlukin δ
IL-δR:		Interleukin δ receptor
IL-λ:		Interlukin λ
IU/d:		International unit/day
J$\gamma\gamma\epsilon$.λ and RAW$\gamma\delta\epsilon$.γ cells :	RAW $\gamma\delta\epsilon$. γ and J $\gamma\gamma\epsilon$. λ	macrophage-like cell lines
JNKλ:		C-Jun N-terminal kinase λ or Stress-activated protein kinase λ
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-acetyl 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[•]:		Nitric oxide.
NOS-γ:		Nitric oxide synthase-γ
O.D.:		Optical Density.
O^{•γ}:		Singlet oxygen .
O^{-γ}:		Superoxide .

OFR :	Oxygen free radicals .
OH.:	Hydroxyl
PAO :	Phenylarsine oxide .
PBMCs:	Prepherial blood mononuclear cells
PCV:	Packed cell volume .
pH:	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^{۲۲۲}:	Radon ۲۲۲
RNA:	Ribonucleic acid
RnDP:	Radon daughtu product
RO:	Alkoyxl radical
RO_۲:	Peroxyl .
RO_۱:	Peroxyl radical
ROS:	Reactive Oxygen Species
S.VCAM-۱:	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^{۹۰}:	Strontium-۹۰.
TACE :	TNF- α converting enzyme .(for TNF see below)
TAD:	Total annual dose

TPR:		Transporter protein receptor
TGFB:		Transforming growth factor B
Th₁:		T helper cell - ١
Th_٢:		T.helper cell - ٢
Th^{٢٣١}:		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^{٢٣٨}:		Uranium ٢٣٨
U^{٢٣٩}:		Uranium ٢٣٩
UF_٦:		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
α-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 – 2 (IL-2), serum IL-6, serum TNF- α levels were determined pre and post triple antioxidants (TAC) administration of Silymarin, in a total daily dose of 210 mg divided into 3 doses. (As Legalon 70 mg three times /day). Selenium, 200 -300 μ g per day (As selenium 100, One capsule twice a day) and Vitamin E, 40 mg per day (As α -tocopherol, One capsule twice a day), for 12 months in 20 uranium miners working 2-10 years (group II), 20 uranium miners working ≥ 10 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 20 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-2, IL-6 and TNF- α , while blood GSH was significantly elevated as compared to control group (group I).

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 238 (U^{238}) among Egyptian uranium miners.