"Study of The Potential Protective Effect of Gonadotropin Releasing Hormone Antagonist on Gamma Radiation Induced Ovarian Failure"

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Submitted By

Dalia Ali Tamim Mohamed

Bachelor Degree in Pharmacy, Faculty of Pharmacy, Ain Shams University (2009)
Researcher Pharmacist at National Center for Radiation Research and Technology, Atomic Energy Authority, Cairo, Egypt

Supervision Committee

Prof.Dr. Ahmed Shafik Nada

Professor of Physiology
National Center for Radiation Research and Technology
Atomic Energy Authority

Prof.Dr. Nadia Hamdy El-Hefny

Professor of Biochemistry
Biochemistry Department
Faculty of pharmacy
Ain Shams University

Ass. Prof. Dr. Mohamed Mostafa Kamal

Associate Professor of Biochemistry
Ain Shams University and
British University in Egypt

Biochemistry Department
Faculty of Pharmacy
Ain Shams University

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بسم الله الرحمن الرحيم

" يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ "

صدق الله العظيم

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Abbreviation	**Refer to**
AMH	Anti-Müllerian Hormone
Apaf-1	Apoptotic protease activating factor 1
BAX	B-Cell Lymphoma 2 Associated X protein
BCL-2	B-Cell Lymphoma 2
BSA	Bovine Serum Albumin
CL	Corpus Luteum
COS	Controlled Ovarian Stimulation
DMSO	Dimethyl SulfoOxide
DNTB	Dithiobis 2-Nitrobenzoic acid
E_2	17-β Estradiol
ELISA	Enzyme Linked Immunosorbant Assay
FSH	Follicle Stimulating Hormone
GCs	Granulose Cells
GnRH	Gonadotropin Releasing Hormone
GnRH-a	Gonadotropin Releasing Hormone agonist
GnRH-ant.	Gonadotropin Releasing Hormone Antagonist
GnRHR	Gonadotropin Releasing Hormone Receptor
GPx.	Glutathione Peroxidase
GR	Glutathione Reductase
GSH	Glutathione reduced
GSSH	Glutathione oxidized
GSTs	Glutathione Transferases
Gy	Gray

Abbreviation	**Refer to**
HIF-1	Hypoxia Inducible Factor 1
HRP	Horseradish Peroxidase
IMM	Inner Mitochondrial Membrane
IR	Ionizing Radiation
IVF	*in vitro* Fertilization
KDR	Kinase insert Domine-containing Region
LD_{20}	Lethal Dose 20
LH	Lutinizing Hormone
MDA	Malon DiAldehyde
OHSS	Ovarian Hyperstimulation Syndrome
OS	Oxidative stress
P	Progesterone
PCNA	Proliferating Cell Nuclear Antigen
POF	Premature Ovarian Failure
ROS	Reactive Oxygen Species
S	Stroma
SC	Subcutaneous
TBA	ThioBarbioturic Acid
TBS	Tris Buffered Saline
TCA	TriChloroacetic Acid
TMB	TetraMethyl Benzidine
VEGF	Vascular Endothelia Growth Factor
VEGFR	Vascular Endothelia Growth Factor Receptor

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Most multi-chemotherapeutic agents can affect oocytes, granulosa cells (GCs), and theca cells, which is detrimental to ovarian reserve and can induce reversible amenorrhea ***(Chuai et al. 2012).*** Also, radiotherapy is a well-known cause of ovarian damage that accelerates menopause leading to permanent infertility ***(Adriaens et al. 2009)***. Although the damage induced is reversible in some tissues, it is progressive and permanent in the ovary ***(Stroud et al. 2009)***. It has a profound impact on ovarian function cases, leading to depletion of the primordial follicle reserve, premature amenorrhea, loss of fertility during or shortly after completion of irradiation ***(Stroud et al. 2009)***. Because none of the currently available methods for ovarian protection and fertility preservation guarantees future fertility ***(Gurgan et al. 2008)***, the need for more effective radioprotectors has been intensified.

Premature ovarian failure (POF) is a common cause of infertility in women and is characterized by amenorrhea before the age of 40-years. It is also known as premature menopause or premature ovarian insufficiency. Actually, it is defined by the presence of menopausal-level serum follicle stimulating hormone (FSH) in women younger than 40 years ***(Welt 2008; Rebar 2009).*** Unexplained POF occurs in up to 1% of the world's female population ***(Skillern and Rajkovic 2008)***; it is associated with loss of fertility, which in most cases is due to the absence of follicles, and in other cases, to the inability of remaining follicles to respond to stimulation ***(Nelson 2009).*** Nevertheless, the currently used cancer therapies are often detrimental to fertility ***(Andersen et al. 2012; Said et al. 2016).***

Cetrorelix is a well-known gonadotropin releasing hormone antagonist (GnRH-ant) which produces immediate and dose-related