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

A thesis submitted for the partial fulfillment of Master's Degree in Pharmacy (Biochemistry)

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بسم الله الرحمن الرحيم
" يَرْفَعِ اللَّهُ الَّذِينَ آَمَنُوا مِنْكُوْ وَالَّذِينَ "
أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ
أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ
فَيِيرُ "

حدق الله العظيم

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Subject	Page
LIST OF ABBREVIATIONS	I
LIST OF TABLES	III
LIST OF FIGURES	V
1. INTRODUCTION AND AIM OF THE WORK	1
2. LITERATURE REVIEW	4
Ovarian Development	4
Premature Ovarian Failure	6
Endocrine Aspects of Ovarian Reserve	8
Ovarian Dysfunction due to Radiation Therapy	13
Mechanism of Radiation-Induced Tissue Damage	14
Radiation-Induced Apoptosis in Ovary	17
	20
Biochemical Diagnosis of POF	21
Techniques of Ovarian Preservation in Cancer Patient	22
GnRH-agonist and antagonists difference.	23
Cetrorelix	25
Pharmacokinetics	27
Pharmacodynamics	29
3. MATERIALS AND METHODS	31
MATERIALS	31
METHODS.	35
Statistical Analysis.	70
4. RESULTS	71
5. DISCUSSION	95
6. SUMMARY AND CONCLUSIONS	104
7. RECOMMENDATIONS	108
8. REFERENCES	109
APPENDIX	i
ARABIC SUMMARY	1_4

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

Table	T:41 a	Dana
No.	Title	Page
1	Effect of cetrorelix injection on circulating hormone levels in rats exposed to whole-body irradiation	74
2	Effect of whole-body irradiation and/or cetrorelix injection on the number of different types of ovarian follicles	76
3	Effect of cetrorelix injection on oxidative stress and lipid peroxidation contents in rats subjected to whole-body irradiation.	81
4	Effect of cetrorelix injection on ovarian BAX, BCL-2 and BAX/BCL-2 in rats subjected to whole-body irradiation	90
5a	Individual data of control group (rats s.c injected with vehicle [DMSO/saline] for 10 days)	i
5b	Individual data of control group (rats s.c injected with vehicle [DMSO/saline] for 10 days)	ii
6a	Individual data of radiation group (rats s.c injected with vehicle [DMSO/saline] for 10 days then exposed to 3.2 gy [dose rate 0.48 gy /min] γ-whole body irradiation after 24 hr from last injection)	iii
6b	Individual data of radiation group (rats s.c injected with vehicle [DMSO/saline] for 10 days then exposed to 3.2 gy [dose rate 0.48 gy /min] γ-whole body irradiation after 24 hr from last injection)	iv
7a	Individual data of cetrorelix group (rats s.c injected with cetrorelix [0.5 mg/kg/day] for 10 days)	v
7b	Individual data of cetrorelix group (rats s.c injected with cetrorelix [0.5 mg/kg/day] for 10 days)	vi
8a	Individual data of cetrorelix/IR group (rats s.c injected with cetrorelix [0.5 mg/kg/day] for 10 days then exposed to 3.2 gy [dose rate 0.48 gy /min] γ-whole body irradiation after 24 hr from last injection)	vii

8b	Individual data of cetrorelix/IR group (rats s.c injected with cetrorelix [0.5 mg/kg/day] for 10 days then exposed to 3.2 gy [dose rate 0.48 gy /min] γ-whole body irradiation after 24 hr from last injection)	viii
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Figure No.	Title	Page
1	Different developmental stages of a follicle.	5
2	The hypothalamic–pituitary–gonadal axis	8
3	Effect of endocrine hormones on various types of ovarian follicles in the ovary.	11
4	Anti-Mullerian hormone pathway	13
5	Action pathways of radiation on DNA	15
6	Apoptosis is triggered through DNA damage by radiation or chemotherapy.	19
7	Signaling mechanisms involved in VEGF-induced angiogenesis	21
8	Mechanism of action of GnRH agonist and antagonist on pituitary receptors.	24
9	Chemical structure of GnRH and cetrorelix acetate	26
10	Standard curve of AMH	37
11	Standard curve of estradiol	40
12	Standard curve of FSH	44
13	Thecal cell development and function during folliculogenesis	46
14	Standard curve of BAX	60
15	Standard curve of BCL-2	64
16	Standard curve of VEGF	69
17	Effect of cetrorelix on serum AMH level (ng/ml) in rats exposed to whole-body irradiation	71
18	Effect of cetrorelix on serum E <sub>2</sub> level (pg/ml) in rats exposed to whole-body irradiation.	72
19	Effect of cetrorelix on serum FSH level (ng/ml) in rats exposed to whole-body irradiation	73

Figure		
No.	Title	Page
20	Ovarian morphometric analysis of ovarian follicles	77
21	Representative photomicrographs of H&E stained ovarian tissue sections.	79
22	Effect of cetrorelix on ovarian oxidative stress and lipid peroxidation content in rats exposed to whole-body irradiation	82
23	Cytochrome c expression in ovarian tissues using immunohistochemical staining.	84
24	Effect of cetrorelix on ovarian cytochrome c expression OD quantification in rats exposed to whole-body irradiation	85
25	Caspase 3 expression in ovarian tissues by immunohistochemical staining	87
26	Effect of cetrorelix on ovarian caspase 3 expression OD quantification in rats exposed to whole-body irradiation	88
27	Effect of cetrorelix on ovarian BAX/BCL-2 ratio in rats exposed to whole-body irradiation	89
28	Immunohistochemical localization of PCNA in ovarian follicles.	92
29	Effect of cetrorelix on ovarian PCNA expression OD quantification in rats exposed to whole-body irradiation	93
30	Effect of cetrorelix on ovarian VEGF expression in rats exposed to whole-body irradiation	94

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