



Role of novel anticancer drug Roscovitine on enhancing radiosensitivity in carcinoma cell lines

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I declare that this thesis has been composed by me and the research work conducted there in has not been submitted for a degree at this or any other university.

Hayan Mostafa Sayed Mohamed

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Whom, I owe an endless love and gratitude for his support
and encouragement during these years.

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Arabic summary
Arabic Abstract

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Abstract

The present study was conducted to evaluate the radiosensitization effect of Roscovitine (cyclin dependent kinase inhibitor) in carcinoma cell lines. Three cell lines are used (HepG2 liver carcinoma cell line, U251 brain carcinoma cell line, H460 Lung carcinoma cell line) in this study .cells were treated with Roscovitine in different concentrations ranging from 0.1 μ M to 100 μ M before exposure to radiation doses ranging from 0.5 Gy to 20 Gy according to each experiment.

The cell viability by MTT assay, The cell cycle analysis by flow cytometry and DNA fragmentation repair mechanism by diphenylamine were measured after Roscovitine treatment with or without radiation to explore the sensitization effect of Roscovitine.

The present study conclude that Roscovitine a good candidate as radiosensitizer for modifying the ionizing radiation (IR) response in cancer cells, beside its cyclin dependent kinase inhibitor function, roscovitine can generate DNA Double strand Breaks and cooperate to enhance IR induce DNA damages . Roscovitine is currently in clinical trials, although our findings suggest that the combination of Roscovitine with IR appears to be a very promising especially for liver, brain and lung cancer

treatment, further investigation is needed to evaluate the therapeutic index before tested in clinical trials.

List of Abbreviations

ATM	: Ataxia telangiectasia mutated
ATP	: Adenine tri phosphate
BSO	: Buthionine sulphoximine
Cdks	: Cyclin-dependent kinases.
Cip/Kip	: Cyclin inhibitor protein / kinases inhibitor protein
DI	: DNA index
DMSO	: Dimethyl sulphoxide
DNA	: Deoxyribonucleic acid
DNA-PK	: DNA- dependent protein Kinase
DNA-PKcs	: DNA- dependent protein Kinase catalytic subunit
DPA	: Diphenylamine
DSB	: Double strand break
ELISA	: Enzyme-Linked ImmunoSorbent Assay
FBS	: Fetal bovine serum
H460	: Lung carcinoma cell line
HCC	: Hepatocellular carcinoma
HCMV	: Human cytomegalovirus
Hep-G2	: Liver carcinoma cell line
HIV -1	: Human immunodeficiency virus type 1
HSV	: Herpes simplex virus
IC50	: Inhibitory concentration 50
INK4	: Inhibitor kinases 4

IR	: Ionizing radiation
MDM2	: Minute double minute protein
MTT	: 3-[4,5-dimethyl thiazole-2-yl]-2,5 Diphenyl tetrazolium bromide
NaCl	: Sodium chloride
NHEJ	: Non homologous end joining pathway
NR	: Not radiated
NS	: Not significant
PBS	: Phosphate buffer saline
PI	: Propidium iodide
RNase A	: Ribonuclease A
RPMI-1640	: Roswell Park Memorial Institute Medium
TCA	: Trichloroacetic acid
TE buffer	: Tris HCl and EDTA.
TTE solution:	TE buffer and Triton X-100
U251	: Brain Carcinoma cell line
VZV	: Varicella-Zoster Virus

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