Biochemical Studies on the Antitumor Activity of *Ziziphus spina-christi* Extracts on Experimentally-Induced Hepatocellular Carcinoma in Rats

Submitted By

Manar Salah Eldin Abdel Aziz

(B. Sc. in Biochemistry, 2012)

Submitted for fulfillment of Master's degree in Biochemistry

Under Supervision of

Dr. Ahmed M. Salem
Professor of Biochemistry
Faculty of Science
Ain Shams University

Dr. Ahmed Abdel Aziz Sayed
Professor of Biochemistry
Faculty of Science
Ain Shams University

Dr. AlShaimaa Mohamed Taha
Lecturer of Biochemistry
Faculty of Science
Ain Shams University

2019

List of Contents

Acknowledgements

I would first like to thank my thesis advisor ***Dr. Ahmed Mohamed Salem***, *professor of Biochemistry, Faculty of Science, Ain Shams University*.

I would like to express my thanks to ***Dr. Ahmed Abdel-Aziz Sayed****, professor of Biochemistry, Faculty of Science, Ain Shams University, for his help and support.*

I would like to express my gratitude to my supervisor Dr. AlShaimaa M.Taha for the useful comments, remarks and engagement through the learning process of this master thesis. She consistently allowed this paper to be my own work, but steered me in the right direction whenever she thought I needed it.

I would also like to thank Dr. Sayed Abdel Raheem, Prof. Ass. of Histopathology at The Faculty of Medicine, Al Azhar university, Cairo, who were involved in the histopathological studies for this research project.

List of Abbreviations

Abbreviation	Meaning
A	Absorbance
AIH	Autoimmune Hepatitis
AKT	Protein kinase B
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
b.w.	Body weight
BC	Before christ
Bcl-2	B cell lymphoma-2
BSA	Bovine serum albumin
CD44	Cell differentiation molecule 44
CDC42	Cell division control protein 42 homolog
cDNA	Complementary deoxyribonucleic acid
COX	cyclooxygenase
CYP2E1	cytochrome P450
DEAE	Diethyl aminoethyl
DENA	Diethylnitrosamine
DEPC	Diethyl pyrocarbonate
DMSO	Dimethyl Sulfoxide
dNTPs	Deoxyribonucleotide triphosphate
DPPH·	free radical, α, ᾱ -diphenyl-β picrylhydrazyl

ds-DNA	Double stranded DNA
E. coli	*Escherichia coli* (bacteria)
EDTA	Ethylenediamine tetraacetic acid
ERK	Extracellular-signal-regulated kinase
FDA	Food and Drug Administration
GAPDH	Glyceraldehyde 3-phosphate dehydrogenase
GC-MS	Gas Chromatography- Mass Spectroscopy
GFR	Glomerular filtrate rate
GGT	Gamma Glutamyl transferase
GSH	Glutathione
GST	Glutathione S-transferases
H&E	Hematoxylin & Eosin stain
H_2O	Water molecule
H_2O_2	Hydrogen peroxide
HBF4	Normal melanocyte cell line
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HepG2	well-differentiated hepatocellular carcinoma cell line
HGF	Hepatocyte growth factor
HGF/c-MET	Hepatocyte Growth Factor/ Cellular-Mesenchymal Epithelial Transition Factor

IC_{50}	The half maximal inhibitory concentration
IGFBPs	IGF high affinity binding proteins
IGF-IR (Igf-1r)	Insulin-like Growth Factor I Receptor
IL	Interleukin
iNOS	Inducible nitric oxide synthase
IRS	insulin receptor substrate
kDa	Kilo Dalton
LD_{50}	Acute Median Lethal Dose
LOX55	Lipoxygenase
MAPK	mitogen-activated protein kinase
MCF-7	Michigan cancer foundation- 7
MDA	Malondialdehyde
mE	milliEquivalent
mM	Millimole
MMP-9	Matrix metalloproteinase -9
MMPs	Matrix metalloproteinases
mTOR	mammalian target of rapamycin
MTT	3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromidefor
NADPH	Reduced "Nicotinamide adenine dinucleotide phosphate"
NASH	Nonalcoholic steatohepatitis
NC	Normal control

nm	nanometer
NO	Nitric oxide
OH	Hydroxide group
OS	Oxidative stress
p53	Tumor protein p53
PBS	Phosphate buffered saline
PCR	Polymerase chain reaction
PI3K	Phosphoinositide 3-kinase
PKB	protein kinase B
Px	Peroxidase
qRT- PCR	Quantitative real time- polymerase chain reaction
Raf	Rabidly Accelerated Fibrosarcoma
RNA	Ribonucleic acid
RNS	Reactive nitrogen species
ROS	Reactive Oxygen Species
RPMI	Roswell Park Memorial Institute
rRNA	Ribosomal ribonucleic acid
RTK	Receptor tyrosine kinase
SD	Standard deviation
SDS	Sodium dodecyl sulphate
TAC	Total antioxidant capacity
TBA	Thiobarbituric acid

TGF-β	Transforming growth factor beta
TNF-α	Tumor necrosis factor alpha
tRNA	Transfer ribonucleic acid
UDP-GT	UDP-Glucuronosyl transferases
VEGFR1-3	Vascular Endothelial Growth Factor
ZSCL	*Ziziphus spina-christi* leaves

List of Tables

List of Figures