The Protective and Preventive Role of Coenzyme Q10 on the Hepatotoxicity Induced by Exposure to Radiation and Paracetamol in Experimental Animals

Thesis
Submitted to Faculty of Science
Ain Shams University
In Partial Fulfillment of Master Degree in Biochemistry

BY

Mahitab Ibrahim Khalil Arafa
B.Sc. Biochemistry

Under Supervision of

Prof. Dr/ Ibrahim H. Borai
Professor of Biochemistry
Faculty of Science
Ain Shams University

Prof. Dr / Mona A. Elgawish
professor of Biochemistry
National Center for Radiation Research and Technology
Atomic Energy Authority

Dr/ Eman I. Kandil
Lecturer of Biochemistry
Faculty of Science
Ain Shams University

Faculty of Science
Ain Shams University
2010

Abstract

The present study was designed to illustrate the protective and therapeutic effect of coenzyme Q10 (40 mg/kg b.wt day other day for one week) in male rats treated with repeated doses of acetaminophen (200 mg / kg b.wt) daily for 14 days and/or exposed to fractionated doses of γ-irradiation (2Gy day other day up to 6 Gy).

Such effect was evaluated by measuring the activities of the most important free radical scavengers of the antioxidant defense system including reduced glutathione (GSH) in blood, glutathione-S-transferase (GST), superoxide dismutase (SOD), nitric oxide (NO) as well as malondialdehyde content (MDA) as an indicator of lipid peroxidation, in plasma.

Hepatocellular damage was evaluated by aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH). DNA fragmentation was determined in liver tissue homogenate of all groups, besides the histological and histochemical analyses.

The results of the present study revealed that AAP and γ-irradiation (individually or cooperated) have shown increases in ALT and AST activities, as well as NO and

MDA levels and decreases in antioxidants SOD and GSH in addition to GST. Moreover, γ-radiation alone or together with AAP represented some increase in LDH activity, while a reduction in LDH activity was noticed with AAP alone. DNA fragmentation showed mild increase with AAP and γ-radiation (alone or combined), the histological and histochemical analyses confirmed the biochemical results.

Pre and post treatments with CoQ10 ameliorated most of the investigated biochemical parameters and showed development in liver structure and even normal appearance of liver tissue sections histologicaly.

List of contents

LIST OF ABBREVIATIONS

AAP	Acetaminophen(paracetamol)
ADP	Adinosin diphosphate
AIDS	Acquired immune deficiency disease
ALT	Alanine transaminase
AST	Aspartate transaminase
As	Absorbance of the standard sample
At	Absorbance of the test sample
ATP	Adinosin tri-phosphate
b.Wt.	Body weight
Ca^{+2}	Calcium ion
CDNB	1-chloro-2,4dinitrobenzen
CoQ10	Coenzyme Q10 (Ubiquinone)
CoQ10H	Semiquinone (ubisemiquinone)
CoQ10H2	Ubiquinol
CuZnSOD	Copper zinc superoxide dismutase
DNA	Deoxyribonucleic acid
DNPH	Dinitrophenyl hydrazine
DSBs	Double-strand breaks
DTNB	5, 5`-dithio- bis (2-nitrobenzoic acid)
e^{-}	Electron
EDTA	Ethylene diamine tetra acetic acid
ETC	Electron transport chain
FDA	Food and Drug Administration of USA
FeSOD	Iron superoxide dismutase
GIT	Gastrointestinal tract
GSH	Reduced glutathione
GS	Glutathione synthase
GSSG	Oxidized glutathione
GST	Glutathione-S-transferase

Gy	Gray (unit of radiation)
H^+	Proton
H_2O_2	Hydrogen peroxide
HC	Hyperchromatisation
HCL	Hydrochloric acid
HMG-COA	3 Hydroxy-methyl glutaryl coenzyme
IgG	Immunoglobulin G
IL-10	Interleukin 10
IL-1 β	Interleukin 1 beta.
INF-gamma	Interferon gamma
iNOS	Inducible nitric oxide synthase
I.P	Interperitonial
IR	Irradiated group
LDH	Lactate dehydrogenase
LDL	Low density lipoprotein
LP	Lipid peroxidation
MDA	Malondialdehyde
Mg^2	Magnesium ion
MnSOD	Manganese superoxide dismutase
MPT	mitochondrial permeability transition
NAD	Nicotinamide adenine dinucleotide
NADH	Nicotinamide adenine dinucleotide (reduced form)
NADPH	Nicotinamide adenine dinucleotide phosphate
NAPQI	N-acetyl-p-benzoquinone imine
NE	Nuclear enlargement
NBT	nitroblue tetrazolium
NF-κB	Nuclear factor –kappa B

NO	Nitric oxide
NOx	nitrite /nitrate
$O2^{\bullet -}$	Superoxide
$OH^{\bullet}$	Hydroxyl radical
$ONOO^{-}$	Peroxynitrite
O.D.	Optical density
Pi	Phosphate
RBCs	Red blood corpuscles
RILD	Radiation-induced-liver-disease
RNA	Ribonucleic acid
ROS	Reactive oxygen species
r.p.m	Rotation per minute
-SH	Sulfhydryl group
SOD	Superoxide dismutase
SSBs	Single strand breaks
TBA	Thiobarbituric acid
TCA	Trichloroacetic acid
TNF-α	Tumor necrosis factor alpha
TQ10	Total Q10
VCL_3	Vanadium trichloride
VLDL	Very low density lipoproteins
DPN	Diphenyl amine

List of figures

List of tables

Acknowledgement

First and foremost thanks to ***Allah,*** the most merciful for guiding me through and giving me strength to complete this work.

I would like to express my deepest gratitude to ***Professor Dr. Ibrahim Hassan Borai,*** Professor of Biochemistry, Biochemistry Department Faculty of Science, Ain Shams University for his kind guidance, valuable advice and instructive criticism and who sacrificed a good deal of his valuable time throughout this work. Without his generous and valuable assistance, this work would lose its value. It is an honor working under his supervision.

I am greatly indebted to ***Professor Dr.Mona Ahmed Elgawish,*** Professor of Biochemistry, National Center for Radiation Research and Technology (NCRRT), Atomic Energy Authority, I'd like to express my deepest respect to her and how honored I am for just being her student, she is a kind of people, one only dreams to be like, I want to thank her for standing by me all along and being my ideal, she spent a big deal of her time with me, in spit of her busy