The Possible Protective Effect of Some Antioxidants on Chemically Induced Hepatocarcinoma in Rats

Thesis Presented By

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For Partial Fulfillment of Master Degree
in Pharmaceutical Sciences
(Biochemistry)

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Approval Sheet

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Contents

Abbreviations

ALT	Alanine aminotransferase
AIF	Apoptosis-inducing factor
AST	Aspartate aminotransferase
CFH	Chlorofluorohydrocarbons
Cys	Cysteine
DEN	Diethylnitrosamine
DHLA	Dihydrolipoic acid
GGT	Gamma- glutamyl-transferase
Ge	Germanium
GR	Glutathione reductase
GST	Glutathione-S-transferase
GSH	Glutathione
GSSG	Glutathione disulfide or Oxidized glutathione
GSH-Px	Glutathione peroxidase
HBV	Hepatitis B Virus
HCC	Hepatocellular carcinoma
HBsAg	HB surface antigen
HBc antibodies	HB core antibodies
HCV	Hepatitis C viral
IFN- γ	Interferon gamma
IFN-γ R1	IFN-γ receptor 1
IFN-γ R2	IFN-γ receptor 2
IL	Interleukin
LPO	Lipid peroxidation
LA	Lipoic acid
MHC	Major histocompatability complex
MDA	Malondialdehyde
MnSOD	Mitochondrial superoxide dismutase
NAC	N-acetyl-L-cysteine
NK cells	Natural killer cells
NASH	Non alcoholic steatohepatitis
NAFLD	Non-alcoholic fatty liver disease
PUFA	Polyunsaturated fatty acids

PLGSH-Px	Phospholipid hydroperoxide glutathione peroxidase
RNS	Reactive nitrogen species
Se	Selenium
SOD	Superoxide dismutases
Th	T-helper cells

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Abstract

The present work aimed to study the possible protective effects of some natural and synthetic antioxidant compounds against chemically induced HCC.

This study included 90 albino Western rats divided into the following 6 groups:

1- Control group.
2- Diethyl nitrosamine and Carbon tetrachloride group [DEN+ CCl_4].
3- Lipoic acid group [LA] (100 mg/kg body weight)
4- A mixture composed of cystiene and selenium [Cys+Se] (0.2 mg/kg body weight)
5- A mixture composed of cystiene and germanium dioxide [Cys+ Ge] (75 mg/kg body weight)
6- A mixture composed of cystiene, selenium and germanium dioxide [Cys+Se+Ge] (0.2 mg/kg body weight)

[LA], [Cys+Se], [Cys+Ge] and [Cys+Se+Ge] were administered one week prior to induction of HCC which was induced by injecting each rat with DEN followed by CCl_4 injection.

To investigate for the hepatoprotective and antioxidant effect of the compounds under investigation, the levels of

malondialdehyde (MDA), reduced glutathione (GSH), activities of glutathione peroxidase (GSH-PX), glutathione S-transferase (GST), and glutathione reductase (GR) were measured in liver homogenate. Activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl-transferase (GGT), level of total protein, albumin and gamma interferon (IFN- γ) were measured in their serum. Microscopic histopathological examination of livers was done to confirm the induction of HCC and the possible protective effect of the compounds under investigation.

The present results showed that injection of [DEN+CCl_4] caused an increase in the oxidative stress in the liver as indicated by the increase in MDA, decrease in GSH content, and increase in GR, GST and GSH-PX activities, accompanied by decrease in IFN- γ levels. Adverse changes in the liver histopathological pattern were also observed in this group of rats. Pretreatment of rats with the compounds under investigation caused an improvement in the studied parameters with different degrees. However, LA administration caused a decrease in IFN-γ compared to the control group. This might clarify the beneficial effects of administration of combinations of these elements in ameliorating the adverse effects caused during HCC.