Abstract

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Title of Thesis: Ameliorating effects of curcumin on hepcidin, some immunological and oxidative stress parameters induced by diazinon in male rats.

Diazinon (DZN) is the most widely used organophosphorus (OP) insecticides, especially in developing countries. It is used to control the pests of agricultural crops in addition to control livestock pests; however it has deleterious effects on health for both humans and animals. Hepcidin is an iron-regulating peptide hormone, reflecting a likely role of hepcidin in innate immunity; hepcidin is also induced by inflammation. Thirty six male albino rats were classified randomly into six equal groups. Group (G1) was kept as control, G2 and G3 were administrated a low and high dose of DZN as 17.5 and 35 mg/kg b.w. (1/20 and 1/10 LD_{50}) respectively, over period of 28 days (5 days/week). G4 received curcumin (CUR) as 200 mg/kg diet. G5 and G6 were administrated high and low dose of DZN, respectively and CUR. The obtained results revealed a significant increase in interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) as the proinflammatory cytokines, hepcidin and ferritin, decrease in erythropoietin (EPO), hemoglobin concentration (Hb), red blood cells (RBCs), serum iron and its related parameters in G2 and G3 were detected in comparison with untreated control (G1). Moreover, CUR treated groups (G5 and G6) revealed improvement of these parameters in comparison with those of corresponding groups. Significant decline in total protein (TP), total albumin (TAlb), total globulin (TGlb) together with albumin/globulin ratio (A/G) of G2 and G3 than control. Significant increase in liver, kidney and spleen malondialdehyde (MDA), catalase (CAT), nitric oxide (NO) with decrease in total antioxidant capacity (TAC) and glutathione (GSH) levels in G2 and G3 than control. Also, the obtained results revealed that there was a significant increase in liver and kideny function parameters in G2 and G3. As CUR is antioxidant and has anti-inflammatory effect could rebalance the state of hypoprotenmia associated with hypoalbunemia, and attenuates the oxidative stress. Moreover, upturned in level of liver and kidney function was observed in G5 and G6. The correlation between hepcidin and IL-6, TNF-α, EPO, iron and its related parameters was determined. Histophathological examination revealed degenerative changes in the liver, kidney and spleen tissues in G2

and G3. Meanwhile, CUR alleviates these changes in G5 and G6. In conclusion sub-acute toxicity of DZN induces alteration in some immunological parameters which in turn cause alteration in hepcidin hormone secretion from hepatic cells leading to anemia and CUR administration had a protective effect against these adverse effects of DZN, also alleviate the deleterious biochemical alterations caused by DZN.

Keywords: Hepcidin, Diazinon, IL-6, TNF-α, Hematological parameters, protein electrophoresis, oxidative stress, Curcumin.

List of Abbreviations

A	Absorbance
A/G ratio	Albumin/ globulin ratio
AAP	4-aminophenazone
Ach	Acetylcholine
AChE	Acetyl cholinesterase
Alb	Albumin
ALP	Alkaline phosphatase
ALT	Alanin aminotransferase
AP-1	Activator protein 1
AST	Aspartate aminotransferase
B	Blank
b.w	Body weight
BG	Between Groups
CAT	Catalase
CCl_4	Carbon tetrachloride
CD	Cluster of differentiation
CD4+	T- helper cell
CD8+	T-cytotoxic cell
CNS	Central nervous system
COX-2	Cyclooxygenase
CUR	Curcumin
CV	Central vein
DcytB	Duodenal cytochrome B
DF	Degree of freedom
DHBS	3,5-Dichloro-2-hydroxybenzene sulfonic acid
DMT-1	Divalent metal transporter-1

DNA	Deoxyribonucleic acid
DZN	Diazinon
ELISA	Enzyme-linked immunosorbent assay.
EPO	Erythropoietin
Fe	Iron
FPN	Ferroportin
FPN1	Ferroportin 1
GDF I5	Growth differentiation factor 15
GFAP	Glial Fibrillary Acidic Protein
GOT	Glutamic oxaloacetic transaminase.
GPT	Glutamic pyruvic transaminase.
GSH	Glutathione
GSH-Px	GSH peroxidase
GSSG	Glutathione disulfide
H&E	Hematoxylin and eosin
Hb	Hemoglobin
HCP1	Heme carrier protein 1
HCT	Haematocrit
HEPH	Ferroxidase hephaestin
HMGB1	High mobility group box-1 protein
HO-1	Heme oxygenase 1
Hrs	Hours
HSCs	Hepatic stellate cells
ICAM-1	Intracellular adhesion molecule-1
IFN- γ	Interferon-gamma
IL	Interleukin
IL-1β	Interleukin-1β
IL-6	Interleukin-6
IMS	Intermediate syndrome

iNOS	Inducible NO synthase
JAK	Janus kinase
LD	Lethal dose
LDH	Lactate dehydrogenase
LPS	Lipopolysaccharide
LYM %	Lymphocyte percent
MAPK	Mitogen-activated protein kinases
MCH	Mean corpuscular Hb
MCHC	Mean corpuscular Hb concentration
MCP-1	Monocyte chemoattractant protein-1
MCV	Mean corpuscular volume
MDA	Malondialdehyde
MDH	Malate dehydrogenase
MHC	Major histocompatibility complex
Min	Minute
mRNA	Messenger ribonucleic acid
NADPH	Nicotinamide adenine dinucleotide phosphate
NF-κβ	Nuclear factor kappa beta
NO	Nitric oxide
NOS	Nitric oxide synthase
NRAMP-1	Natural resistance-associated macrophage protein 1
OD	Optical density
OP	Organophosphorus
OPs	organophosphates
PBS	Phosphate buffer saline
PBS-T	PBS-Tween
PCV	Packed cell volume
PLT	Platelet
PMA	Phorbol 12-myristate 13-acetate

PON1	Paraoxonase/arylesterase1
PR	Precipitating Reagent
PreAlb	Pre Albumin
PV	Portal veins
r	Correlation coefficient
R.T	Room temperature
RBCs	Red blood cells
ROS	Reactive oxygen species
S	Standard
SB	Sample blank
Sec	Seconds
SEM	Standard error of mean
SR	Saturating Reagent
STAT3	Signal transducer and activator of transcription 3
T	Test
TAC	Total antioxidant capacity
TAlb	Total Albumin
TBA	Thiobarbituric acid
TF	Transferrin
TfR1	Transferrin receptor
TGlb	Total globulin
TIBC	Total iron binding capacity
TLR	Toll-like receptors
TLR2	Toll-like receptor2
TLR4	Toll-like receptor 4
TMB	Tetra methyl benzidine.
TNF-α	Tumor Necrosis Factor-alpha
TP	Total protein
TRAIL	TNF-related apoptosis-inducing ligand

TWSGI	Twisted gastrulation I
Tα	Total alpha
Tβ	Total beta
Tγ	Total gamma
UIBC	Unsaturated iron binding capacity
WBCs	White blood cells
WG	Within Groups
α1	Alpha 1
α2	Alpha 2
α2-M	Alpha-2-Macroglobulin
β1	Beta 1
β2	Beta 2
γ1	Gamma 1
γ2	Gamma 2

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