

Dedicated to my parents
My Abba Alhaj Jalal Uddin
And
Maa Saira Begum

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Date:

Place:

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PREFACE

Heavy metals have been playing a critical role in industrial development and technological advances. Most of the metals are not destroyed rather, they tend to accumulate at an accelerated pace due to the ever growing demands of modern society. The wide spread distribution of metals in the environment is of great concern because of their toxic properties. Heavy metals are some of the major contaminants whose concentrations in the environment should be kept low due to their toxic nature. Heavy metals are serious pollutants of the aquatic environment because of their environmental persistence and ability to be accumulated by aquatic organisms. Unlike organic pollutants, heavy metals do not decay and thus pose a different kind of challenge for remediation.

Fish are generally appreciated as one of the healthiest and cheapest sources of protein and it has amino acid compositions that are higher in cysteine than most other sources of protein. Prolonged exposure to heavy metals such as mercury, cadmium, copper, lead, nickel, and zinc can cause deleterious health effects in humans. Fish are important components of human nutrition, and those from contaminated sites present a potential risk to human health. Therefore a balance is to be maintained between heavy metals in the aquatic environment and human health.

The scientific pursuit of toxicology is typically divided in to observational studies- looking at what effects results from an exposure to a particular substance and experimental studies which attempt to understand mechanism and explain the basis for such effects. These two activities form the basis of toxicology as an experimental science which takes place in the laboratory or occasionally in the field.

The current piece of work is an original investigation undertaken to acquire new knowledge directed towards specific aims or objectives. This is an assimilation of three different attempts blended in to a single work in order to resolve certain queries. The following episodes represent the overall process in harnessing a curiosity on the toxicity of mercury and cadmium on the intestinal macrophages of *Channa punctatus* after short term (4 days and 7 days respectively) exposure.

The investigation initiated with an *in vivo* approach which focused on the effect heavy metals mercury and cadmium. This chapter provides a critical assessment of toxicological effects of single metal exposure on the ultra structural changes, oxidative stress, antioxidant defenses and innate immune system on the intestinal macrophages of *Channa punctatus* for 4 days and 7 days of exposure.

Interestingly, in the next stage of the study, it was observed that there was a synergistic effect after the mutli-metal exposure that means the exposure of mercury and cadmium in combination in the antioxidant defenses and innate immune response after 4 days and 7 days of exposure.

In the 3rd stratum, in concurrence with this research work is an attempt to predict the molecular mechanism of toxicity based on the mRNA expression levels after the 7 days of exposure of mercury and cadmium exposure in single and in combination which established a good relation between oxidative stress, antioxidant defenses and innate immune system. Thus this thesis is an amalgamation of three prolonged approaches which provide an overview of how these heavy metals have a deleterious effect on non- specific host defenses in *Channa punctatus*.

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List of Abbreviations

AAS: Atomic absorption spectroscopy

ATP : Adenosine tri-phosphate

C3 component: Complement component 3

CAT: Catalase

Cd: Cadmium

CRP: C- reactive protein

DNA: Deoxyribonucleic acid

GI: Gastro-intestinal

GPx: Glutathione peroxidase

GR: Glutathione reductase

GSH: Reduced glutathione

GST: Glutathione-S-transferase

H₂O₂: Hydrogen peroxide

Hg: Mercury

HOCl: Hypochlorous acid

IL-6: Interleukin 6

iNOS: Nitric oxide synthase

LPO: Lipid peroxidation

MAF: Macrophage activating factor

MDA: Malondialdehyde

MPO: Myeloperoxidase

NADPH: Nicotinamide adenine dinucleotide phosphate

NK cells : Natural killer cells

NO: Nitric oxide

PAMPs: Pathogen associated molecular patterns

PI: Phagocytic index

qRTPCR: Quatitative reverse transcription polymerase chain reaction

RB: Respiratory burst

RNS: Reactive nitrogen species

ROS: Reactive oxygen species

SEM: Scanning electron microscopy

-SH: -Sulphydryl group

SOD: Superoxide dismutase

TEM: Transmission electron microscopy

TLR: Toll-like receptor

TNF- α : Tumor necrosis factor-alpha

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