

**DETERMINATION OF SOME ENVIRONMENTAL TOXINS
THAT MIGHT CAUSE LIVER CANCER IN FOOD**

Submitted By

Hend Mohamed Ali Ahmed

B.Sc. of Science (Chemistry/Microbiology), Faculty of Science, Assuit University, 2007

Diploma in Biochemistry, Faculty of Science, El Minia University, 2009

Diploma in Environmental Sciences, Institute of Environmental Studies & Research,
Ain Shams University, 2015

A thesis submitted in Partial Fulfillment
Of
The Requirement for the Master Degree
In
Environmental Sciences

Department of Environmental Basic Sciences
Institute of Environmental Studies and Research
Ain Shams University

2018

APPROVAL SHEET

DETERMINATION OF SOME ENVIRONMENTAL TOXINS THAT MIGHT CAUSE LIVER CANCER IN FOOD

Submitted By

Hend Mohamed Ali Ahmed

B.Sc. of Science (Chemistry/Microbiology), Faculty of Science, Assuit University, 2007

Diploma in Biochemistry, Faculty of Science, El Minia University, 2009

Diploma in Environmental Sciences, Institute of Environmental Studies & Research,
Ain Shams University, 2015

A thesis submitted in Partial Fulfillment
Of

The Requirement for the Master Degree
In

Environmental Sciences

Department of Environmental Basic Sciences

This thesis Towards a Master Degree in Environmental Sciences Has
been Approved by:

Name

Signature:

1-Prof. Dr. Mahmoud Ahmed Ibrahim Hewaihy

Prof. of Public Health, Department of Environmental Basic Sciences
Institute of Environmental Studies & Research
Ain Shams University

2-Prof. Dr. Nafisa Mostafa Eid

Prof. of Industrial Foods
National Nutrition Institute

3-Prof. Dr. Taha Abd El Aziem Mohamed Abd El- Razek

Prof. of Environmental Chemistry, Vice Dean of Institute of Environmental
Studies & Research for Environment & Community Affairs
Ain Shams University

4-Prof. Dr. Hanaa Hussein El Sayed

Prof. of Chemistry Nutrition & Metabolism
National Nutrition Institute

2018

**DETERMINATION OF SOME ENVIRONMENTAL TOXINS
THAT MIGHT CAUSE LIVER CANCER IN FOOD**

Submitted By

Hend Mohamed Ali Ahmed

B.Sc. of Science (Chemistry/Microbiology), Faculty of Science, Assuit University, 2007

Diploma in Biochemistry, Faculty of Science, El Minia University, 2009

Diploma in Environmental Sciences, Institute of Environmental Studies & Research,
Ain Shams University, 2015

A thesis submitted in Partial Fulfillment
Of
The Requirement for the Master Degree
In
Environmental Science
Department of Environmental Basic Sciences

Under The Supervision of

- 1- Prof. Dr. Taha Abd El Aziem Mohamed Abd El-Razek**
Prof. of Environmental Chemistry, Head of Department of
Environmental Basic Sciences - Institute of Environmental Studies
& Research - Ain Shams University
- 2- Prof. Dr. Hanaa Hussein El Sayed**
Prof. of Chemistry Nutrition & Metabolism
National Nutrition Institute
- 3- Dr. Ehab Fawzy Abdou Moustafa**
Associate Prof. of Tropical Medicine and Gastroenterology
Faculty of Medicine
Assuit University

2018

Acknowledgement

First of all, I thank Allah who gave me the strength to fulfill this work. My thanks and deep appreciation to Prof. Dr. Taha A.M. Abd El Razk, Professor of Analytical chemistry; Environmental Institute for Research, Ain Shams University, for his guidance, motivation and support throughout my master thesis. his insight helped me to finish this research in such a good form. I am very thankful that I become one of his students.

Special and great thanks to Prof. Dr. Hanaa H. El Sayed, Professor of environmental science for Chemistry of nutrition and metabolism, National Nutrition Institute, for her great help, guidance, fruitful assistance, encouragement and precious advice given throughout this study.

Also, I will always remember with much appreciation then kind help and co-operation of Prof. Ehab F. A. Moustafa, Professor of Tropical Medicine and Gastroenterology, Assuit University.

Finally, I would like to express my special thanks to my parents, husband, sisters, brothers, sons and friends for their kind help, continuous encouragement, understanding and support that helped me to finish my research in this form.

Abstract

Human are exposed to hepatocarcinogenic aflatoxins through ingestion of foods which exposed to poor storage condition of susceptible grains or eating foods carried aflatoxins from animals and vegetables. This study evaluated the effect of total aflatoxin on liver health of subjects. Ninety Subjects were divided into three groups (each /30 Subjects). Group (1) not suffering liver disease as normal or negative control. Group (2) patients input/or output (El Raghi hospital in Assuit) are suffering of hepatocellular carcinoma (HCC). Group (3) patients input (El Raghi hospital in Assuit) are suffering of liver inflammatory disease (HI). This study used 24 h recall and food frequency questioners for these groups to determination the type and amount of food which were intake. Random samples were obtained of some foods frequency intake as a source of protein (chicken egg; chicken, duck and rabbit liver) purchased from local market in Assuit; which determined total amount of aflatoxins using high- performance liquid chromatography (HPLC). In serum was measured Aflatoxin Albumin Adduct (AAA) by enzyme-linked immunosorbent assay (ELISA) kites and used colorimetric kites to determine liver function (Alanine transaminase (ALT), Aspartate transaminase (AST), Total protein (TP), albumin (Alb), Bilirubin (Total,

Direct), alkaline phosphatase (ALP), Glutathione peroxidase (GPX) and Malondialdehyde (MDA) by used spectroscopy instrument. Study detected a correlation between ALT, GPx, MDA, and AAA in human. Study concluded that these alterations in liver functions could be related to the development of liver damage in response to significant dose of Aflatoxins.

Key words: Aflatoxins- health of humans- liver disease.

List of Contents

<i>No.</i>	<i>Title</i>	<i>Pages No.</i>
<i>1</i>	List of tables	II
<i>2</i>	List of Figures	III
<i>3</i>	List of abbreviations	IV
<i>4</i>	Introduction	1
<i>5</i>	Aim of work	3
<i>6</i>	Literature Review	4
<i>7</i>	Subjects, Materials and Methods	54
<i>8</i>	Results and Discussion	67
<i>9</i>	Conclusion	80
<i>10</i>	Recommendation	81
<i>11</i>	Summary	82
<i>12</i>	References	85
<i>13</i>	Appendices	114

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
<i>Table (1)</i>	Characteristic of the study groups.	67
<i>Table (2)</i>	Value of Aflatoxin content (ppb) in eggs and liver	69
<i>Table (3)</i>	Food intake of different patients from some food contain aflatoxins, mean \pm SE (g /d)	72
<i>Table (4)</i>	Glutathione peroxide, Aflatoxin Albumin Adduct and Malondialdehyde in serum study groups	74
<i>Table (5)</i>	Liver function parameters in serum study groups	76
<i>Table (6)</i>	Correlations Group HCC	78

List of Figures

<i>Fig. No.</i>	<i>Title</i>	<i>Page No.</i>
<i>Figure (1)</i>	Overview of aflatoxin pathway to humans	5
<i>Figure (2)</i>	Structure of aflatoxins	9
<i>Figure (3)</i>	Metabolism of aflatoxin in liver	17
<i>Figure (4)</i>	Location of liver	26
<i>Figure (5)</i>	Vascular and architectural alterations in cirrhosis	40
<i>Figure (6)</i>	Sex distribution in study groups.	68
<i>Figure (7)</i>	Value of Aflatoxins in eggs and livers (chicken, rabbit and duck).	70
<i>Figure (8)</i>	Food intake of different patients from some food contains Aflatoxins.	73
<i>Figure (9)</i>	Correlation between ALT & Aflatoxin in HCC group.	78
<i>Figure (10)</i>	Correlation between AST & Aflatoxin in HCC group.	79

List of Abbreviations

AAA	Aflatoxin Albumin Adduct
AFL	Aflatoxins
AFT-B ₂	Aflatoxin B 2
AFT-G ₁	Aflatoxin G 1
AFT-G ₂	Aflatoxin G 2
Alb.	Albumin
ALP	Alkaline phosphatase
ALT	Alanine transaminase
AST	Aspartate transaminase
TP	Total protein
BCG	Bromocrasol green
D. Bilirubin	Direct Bilirubin
FAO	Food and Agricultural Organization
FDA	Food and Drugs Administration
GGT	Gamma-glutamyl transferase
GMP	Good manufacturing practices
GR	Glutathione reductase
GPIS	Grain and Plant Inspection Service
GPx	Glutathione peroxidase
HACCP	Hazard analysis of critical control points

HSC	Hepatic stellate cells
IFCC	International Federation of Clinical Chemistry
LDH	lactate dehydrogenase
MDA	Malondialdehyde
MDH	Malate dehydrogenase
NAC	N-acetyl-L-cysteine
NAFLD	non-alcoholic fatty liver disease
NAPQI	N-acetyl -P- benzoquinoneimine
OTC	over-the-counter
NNI	National Nutrition Institute
PCBs	polychlorinated biphenyls
p-NPP	p-Nitrophenylphosphate
SPE	Solid Phase Extraction
TBA	Thiobarbituric acid
T. Bilirubin	Total Bilirubin
TFA	Trifluoroacetic acid
USFDA	United States Food and Drug Administration
VOCs	Volatile Organic Compounds
WHO	World Health Organization
ZEA	Zeranol

Introduction

1 Introduction

(WHO, 2014) reported that there are lots of environmental toxins in our air, water and/or food supply affecting of humans health. Food contamination is a public health problem that is monitored worldwide. (Fehizardo and Camara, 2013) found that care in food preparation and storage are so serious to avoid intake of various microorganisms and their toxins.

(Liu and Wu, 2010) showed that aflatoxins are a group of approximately 20 related fungal metabolites. The four major aflatoxins are known as B1, B2, G1, and G2. Aflatoxins B2 and G2 are the dihydro-derivatives of the parent compounds B1 and G1. Aflatoxins refer to serious health, economic and agricultural problems in developing countries (Afum et al., 2016).

(Wild and Turner, 2002) indicated that aflatoxins (AFL) contaminate food during storage, production and processing. Due to their high toxicity and carcinogenic effects, they have long been suggested as possible an etiologic agent of hepatocellular carcinoma (HCC).

(Reddy and Bhoola, 2010) who said that excreted aflatoxins metabolites were related to have an increased risk of HCC.

The adverse health effects of aflatoxins can be categorized as either acute or chronic. Acute aflatoxicosis occurs when moderate to high levels of the toxins are consumed and may result in hemorrhage, acute liver damage, edema of the limbs, alteration in digestion (absorption and/or metabolism of nutrients), high fever, vomiting, swollen livers and possibly death (Verma, 2004).

Chronic aflatoxicosis is results from ingestion of low to moderate levels of aflatoxins and the effects are usually subclinical and difficult to recognize **(CDC, 2004)**.

(WHO, 2014) reported that liver cancer is the sixth most common cancer worldwide, with 782,000 new cases diagnosed in 2012. It is the second most common cause of death from cancer and is more common in men than women. Hepatocellular carcinoma (HCC) accounted for 70% -90% of primary liver cancers, making it the third leading cause of cancer related deaths worldwide **(El-Serag et al., 2007)**.

This study carried out on aflatoxin in some food that may be the cause liver diseases in humans and relation between Aflatoxin in foods and HCC in humans.

Aim of the work