شبكة المعلومات الجامعية

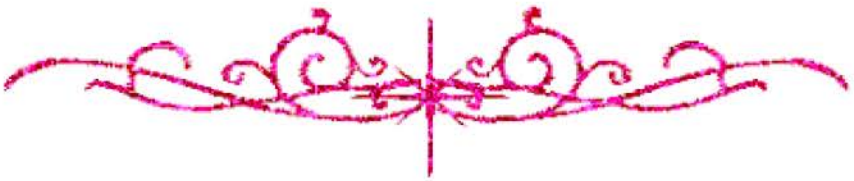
بسم الله الرحمن الرحيم

HOSSAM MAGHRABY

شبكة المعلومات الجامعية

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم



HOSSAM MAGHRABY

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

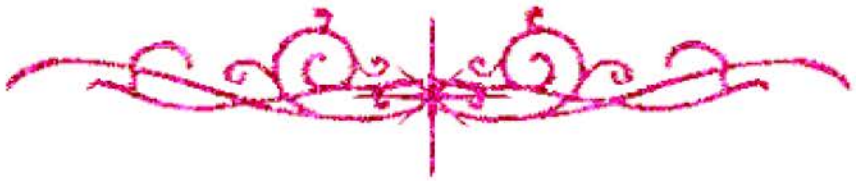
يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

HOSSAM MAGHRABY

شبكة المعلومات الجامعية

بعض الوثائق الأصلية تالفة



HOSSAM MAGHRABY

شبكة المعلومات الجامعية

بالرسالة صفحات

لم ترد بالأصل

HOSSAM MAGHRABY

SCREENING FOR MYCOTOXINS IN CHRONIC LIVER DISEASES

THESIS

Submitted for Partial Fulfillment
of The Requirements for The
MASTER DEGREE IN TROPICAL MEDICINE

By

Sabah Ahmed Sayed

M.B.B.Ch. - Assiut University

Supervised by

Dr. *Abdel Ghani Abdel Hamid Soliman*

Assistant Professor of Tropical Medicine and Gastroenterology

Prof. Dr. *Ismail A.M. El Kady*

Professor of Microbiology,
Faculty of Science, Assiut University

Dr. *Youssef Mohammed Swifee*

Lecturer of Tropical Medicine and Gastroenterology

Faculty of Medicine - Assiut University

1997

بسم الله الرحمن الرحيم

الحمد لله رب العالمين

صدق الله العظيم

To My Parents

CONTENTS

Page

Introduction and Aim of the Work 1

Review of Literature 3

- Aflatoxins 3

* Historical notes 3

* Aflatoxins producing fungi 3

* Prevalence of aflatoxin 4

* Chemistry of aflatoxin 5

* Chemical reaction of aflatoxin 5

* Binding of aflatoxins B_1, G_1 and M_1 to plasma albumin 6

* Mode of action of aflatoxin B_1 7

* Putative Disease Outcomes 8

1- Acute hepatitis 8

2- Hepatocellular carcinoma 9

* Incidence 9

* Age and sex 11

* Role of mycotoxins in pathogenesis of HCC 12

* Aetiological factors in HCC other than mycotoxins 15

1- Hepatitis B virus 15

2- Hepatitis C virus 17

3- Delta agent 20

4- Liver Cirrhosis 20

3- Kwashiorkor 23

4- Reye's Syndrome 24

5- Liver cirrhosis 25

6- Other aflatoxin related diseases 25

- Ochratoxins 25

- Tricothecences 26

Page

- Zearalenone 28
- Sterigmatocystin 28

Patients and Methods 30

Results 36

Discussion 43

Summary and Conclusions 49

References 51

Arabic Summary .....

ABBREVIATIONS

AF-alb	Aflatoxin-albumn adduct
AFB_1	Aflatoxin B_1
AFP	Alpha fetoprotein
ALT	Alanine transaminase
Anti-HC	Hepatitis C antibody
ATA	Alimentary toxic aleukia
CLD	Chronic liver diseases
DNA	Deoxy ribonucleic acid
EIA	Enzyme immuno assay
ELISA	Enzyme linked immunosobant assay
FAO	Food and Agricultural Organization of United Nations
HBs Ag	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HPLC	High performance liquid chromatography
HCV	Hepatitis C virus
IARC	International agency for research on cancer
MFO	Microsomal mixed-function-oxidase
PHC	Primary hepatocellular carcinoma
RIA	Radio immuno assay
RNA	Ribonucleic acid
TLC	Thin layer chromatography
U.V.	Ultra violet

ACKNOWLEDGMENT

ACKNOWLEDGEMENT

First of all, all gratitude is due to GOD the Almighty who guided and aided me in bringing this thesis to light which would have never been crowned by success without blessing of Allah to whom my faithful loyalty will remain however beyond any compromises.

It is pleasure to express my deepest appreciation, gratitude and sincere thanks to my supervisor, Dr. ***Abdel-Ghani A. Soliman***, Assistant Professor of Tropical Medicine and Gastroenterology, Faculty of Medicine, Assiut University, for his constructive suggestions, excellent guidance and eminent supervision which tided me over the difficulties I met with throughout this work.

I wish to express my deep and extreme appreciation to Prof. Dr. ***Ismail El-Kady***, Professor of Microbiology, Botany Department, Faculty of Science, Assiut University, for his valuable instructions, continuous encouragement and kind support during all steps of implementing this study.

I would like to express my greatest and deepest thanks to Dr. ***Youssef M. Swifee***, Lecturer of Tropical Medicine and Gastro-enterology for his advice, kind help and sincere encouragement.

My thanks and gratitude also go to Dr. ***Enass Abd El-Maguid***, Lecturer of Microbiology, Faculty of Medicine, Assiut University, for her kind help and providing facilities during the practical part of this thesis.

It is my pleasure to express my deep thanks to Dr. ***Ashraf Osman*** and other ***Staff Members*** of Tropical Medicine and Gastroenterology Department, Faculty of Medicine, Assiut University for their valuable and practical assistance.

Sabah Ahmed

INTRODUCTION AND AIM OF THE WORK

INTRODUCTION AND AIM OF THE WORK

Mycotoxins are compounds produced by fungi that are toxic to animals and humans when consumed in foodstuff (Mirocha, 1983).

Humans are exposed to mycotoxins by consumption of commodities that are contaminaled with mycotoxins, or products of animals that have ingested mycotoxin contaminated Fed (Hsieh ,1983).

The mature animals are an effective toxin modifier eliminator (Swenson *et al.,* 1974). The metabolism and trasmission process acts like a filter allowing only a small portion of the toxins to pass through in the form of less toxic metabolites. Thus the toxin present in the feed and the quantity of the metabolites are usually only a few percent of the quantity of the parent toxins. Therefore, the main concern about mycotoxins and their metabolites in animal products are a chronic toxicity of these compounds, especially carcinogenicity, which is a problem resulting from long term low level exposure (Hsieh, 1983).

The most important mycotoxins are aflatoxins, ochratoxins, trichothecenes and zearalenone and other rare types citreoviridin, citrinin, sterigmatocystin and patulin toxins. They produce disease named mycotoxicoses, a broad spectrum of diseases of both acute and chronic nature resulting from the consumption of mycotoxins, have been encountered in humans and livestock in many parts of the world including both developed and developing countries (WHO, 1977).

Aflatoxins are mycotoxins produced by *Aspergillus flavus* or *A. parasiticus* fungi. They are common contaminants of a wide variety of foods in different countries (Goldblatt, 1969). There are 4 major aflatoxins: B_1, B_2, G_1, G_2 and a number of derivatives e.g. M_1, M_2, B_2a Q_1 and aflatoxicol (WHO, 1979).