شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

# بسم الله الرحمن الرحيم


HANAA ALY

# شبكة المعلومات الجامعية

# التوثيق الالكتروني والميكروفيلم

HANAA ALY

شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

# 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

HANAA ALY

**Cairo University**
**Faculty of Veterinary Medicine**
**Department of Toxicology and Forensic Medicine**

# Immuno and Nephrotoxicity of Ochratoxin A on Broiler Chicken and a Trial for Protection

**Thesis Presented by**

## Rehab E. Abdelrahman

(B.V.Sc., Cairo University, 2018)

**To**
Cairo University,
Faculty of Veterinary Medicine,

**For the Master's Degree in Veterinary Medical Sciences**
(Toxicology, Forensic Medicine and Veterinary Regulations)

**Under supervision of**

**Prof. Dr. Abdel-Azeim A. Khalaf**
Professor of Toxicology and Forensic Medicine,
Faculty of Veterinary Medicine, Cairo University

**Prof. Dr. Mohamed A. Elhady**
Professor of Toxicology and Forensic Medicine, Vice Dean for Community Service and Environment Development, Faculty of Veterinary Medicine, Cairo University

**Dr. Peter A. Noshy**
Lecturer of Toxicology and Forensic Medicine, Faculty of Veterinary Medicine, Cairo University

**2021**

**Cairo University**
**Faculty of Veterinary Medicine**
**Department of Toxicology and Forensic Medicine**

# Immuno and Nephrotoxicity of Ochratoxin A on Broiler Chicken and a Trial for Protection

***Thesis Presented by***

**Rehab Essam Abdelrahman**

(B.V.Sc., Cairo University, 2018)

To
Cairo University,
Faculty of Veterinary Medicine,

**For the Master's Degree in Veterinary Medical Sciences**
(Toxicology, Forensic Medicine and Veterinary Regulations)

***Under supervision of***

**Prof. Dr. Abdelazeem Aly Khalaf**
Professor of Toxicology and Forensic Medicine,
Faculty of Veterinary Medicine, Cairo University

**Prof. Dr. Mohammed Aly Elhady**
Professor of Toxicology and Forensic Medicine, Vice Dean for Community Service and Environment Development, Faculty of Veterinary Medicine, Cairo University

**Dr. Peter Azmy Noshy**
Lecturer of Toxicology and Forensic Medicine, Faculty of Veterinary Medicine, Cairo University

**(2021)**

**Cairo University**
**Faculty of Veterinary Medicine**
**Department of Toxicology and Forensic Medicine**

# SUPERVISION SHEET
# SUPERVISORS

## Prof. Dr. Abdelazeem Aly Khalaf

Professor of Toxicology and Forensic Medicine,

Faculty of Veterinary Medicine, Cairo University.

## Prof. Dr. Mohammed Aly Elhady

Professor of Toxicology and Forensic Medicine,

Faculty of Veterinary Medicine, Cairo University.

## Dr. Peter Azmy Noshy

Lecturer of Toxicology and Forensic Medicine,

Faculty of Veterinary Medicine, Cairo University.

**Cairo University**
**Faculty of Veterinary Medicine**
**Department of Toxicology and Forensic Medicine**

**Name** : **Rehab Essam Abdelrahman**
**Degree** : **Master's degree of veterinary science**
**Specification** : **Toxicology, Forensic Medicine and Veterinary Regulations**
**Title** : **Immuno and Nephrotoxicity of Ochratoxin A on Broiler Chicken and a Trial for Protection**
**Supervisors** : **Prof. Dr. Abdelazeem Aly Khalaf**
**Prof. Dr. Mohammed Aly Elhady**
**Dr. Peter Azmy Noshy**

# Abstract

Ochratoxin A (OTA), a wide-spread mycotoxin, is a secondary metabolite of different fungal species such as *Aspergillus* and *Penicillium*. Quercetin (QUE) is one of the flavonoids produced as a plant-secondary metabolite. In this *in vivo* study, we aimed to investigate the efficiency of QUE against dietary OTA-induced immunotoxicity and nephrotoxicity in the broiler chickens. Forty one-day-old broiler chicks were divided randomly and equally into four groups; control, OTA (0.5 mg/kg feed), QUE (0.5 g/kg feed) and OTA + QUE in the same mentioned concentrations. Our results showed a significant decrease in antibodies response against Newcastle Disease, Avian Influenza and Infectious Bronchitis vaccines, as well as the lymphoproliferative response to the injected Phytohemagglutinin-P in the OTA group. Serum biochemical wastes (urea nitrogen, uric acid and creatinine) were significantly elevated after exposure to OTA. Moreover, antioxidants (catalase and reduced glutathione) were significantly reduced and the malondialdehyde content was significantly increased in kidney, bursa of Fabricius, spleen and thymus tissues. Additionally, several pathological lesions were showed in organs of the OTA-receiving group. Ochratoxin A also induced apoptosis that was evident by increased PTEN, BAX and Caspase-3 and decreased PI3K, AKT and Bcl-2 genes levels. On the other hand, administration of QUE ameliorated most of the immunotoxic and nephrotoxic effects of OTA by its immunomodulatory, antioxidant and anti-apoptotic activities. Taken together, the results suggested that QUE potentially alleviated the OTA-induced immunotoxicity and nephrotoxicity in broiler chickens, probably through amelioration of oxidative stress and activation of the PI3K/AKT signaling pathway.

## *Acknowledgement*

*It is a genuine pleasure to express my deep sense of thanks to my supervisor and guide* ***Prof. Dr. Abdel-Azeim A. Khalaf****. His dedication, keen interest to help his students and generous advices had been responsible for completing this work.*

*I would like to give my warmest thanks to my supervisor* ***Prof. Dr. Mohamed A. Elhady*** *who made this work possible despite his overwhelming schedule. His guidance, advice and cooperative response to all my questions with kindness carried me through all the stages of my project.*

*I owe a deep sense of gratitude to* ***Dr. Peter A. Noshy,*** *for his keen interest on me at every stage of my research and letting my work be enjoyable moments. His prompt inspirations, timely suggestions with kindness and enthusiasm have enabled me to complete this work.*

*I would like to express my gratitude to my adviser* ***Prof. Dr. Marwa A. Ibrahim*** *professor of biochemistry and metabolism, faculty of veterinary medicine, cairo university, who is always by my side, for her guidance, cooperative response to all my questions with kindness and accomplishing the molecular tests.*

*My sincere thanks also to* ***Dr. Eman I. Hassanen****, assistant professor of pathology, faculty of veterinary medicine, cairo university, for her kind help in accomplishing the histopathological examinations.*

*I thank profusely all the* ***Staff of the department of Toxicology and Forensic Medicine*** *for their kind help and every single advice throughout this work.*

*Last but not the least; I would like to express my gratitude to my* ***Mother, Father, Sister and Brothers*** *for their unconditional love, continuous support and understanding. Your prayer for me and trust were what sustained me this far…*

# Contents

# List of Tables

# List of Figures

# List of Abbreviations

| | |
|---|---|
| **AI** | Avian influenza |
| **AKT** | Protein Kinase B |
| **BAX** | Bcl-2-associated X protein |
| **BCA** | Bursal cortical area |
| **Bcl-2** | B-cell lymphoma 2 |
| **BEN** | Balkan endemic nephropathy |
| **BUN** | Blood urea nitrogen |
| **CASP-3** | Cysteine-aspartic proteases 3 |
| **CAT** | Catalase |
| **CRE** | Creatinine |
| **ELISA** | Enzyme-linked immunosorbent assay |
| **GIT** | Gastrointestinal tract |
| **GPx** | Glutathione peroxidase |
| **GR** | Glutathione reductase |
| **GSH** | Reduced glutathione |
| **HDL** | High density lipoprotein |
| **HI** | Haemagglutination inhibition |

| | |
|---|---|
| **HL** | Human leukemia |
| **IACUC** | Institutional animal care and use committee |
| **IARC** | International agency for research on cancer |
| **IB** | Infectious bronchitis |
| **LDL** | Low density lipoprotein |
| **MAPK** | Mitogen-activated protein kinase |
| **MDA** | Malondialdehyde |
| **MDCK** | Madin-darby canine kidney |
| **MPN** | Mycotoxic porcine nephropathy |
| **MTC** | Masson’s trichrome |
| **ND** | Newcastle disease |
| **NIH** | National institutes of health |
| **NRC** | National research council |
| **Nrf2** | Nuclear factor erythroid 2-related factor 2 |
| **OAT** | Organic anion transport |
| **OT** | Ochratoxin |
| **OTA** | Ochratoxin A |
| **PAS** | Periodic-acid schiff |

| | |
|---|---|
| **PBS** | Phosphate-buffered saline |
| **PHA-P** | Phytohemagglutinin-P |
| **PI3K** | Phosphatidylinositol 3-kinase |
| **PTEN** | Phosphatase and TENsin homolog deleted on chromosome 10 |
| **QUE** | Quercetin |
| **RNS** | Reactive nitrogen species |
| **ROS** | Reactive oxygen species |
| **RTD** | Renal tubular degeneration |
| **RTN** | Renal tubular necrosis |
| **RTP** | Renal tubular proliferation |
| **SLFA** | Splenic lymphoid follicular area |
| **SOD** | Superoxide dismutase |
| **TBARS** | 2-Thiobabituric acid-reactive substances |
| **TCA** | Thymus cortical area |
| **UA** | Uric acid |