# THE CONSEQUENCES OF THE ADVERSE INTERACTION BETWEEN METHOTREXATE AND TWO NON STEROIDAL ANTIINFLAMMATORY DRUGS

**THESIS** 

SUBMITTED FOR PARTIAL FULFILMENT OF

M.D. in

CLINICAL TOXICOLOGY

By

Einas El-Sayed Mohammed Aboul-Wafa El-Taftazani

M.B.B.Ch. - M.S.

9282

Circle

SUPERVISED BY

Prof. Dr. Naila Ahmed El-Nayal

Prof. of Forensic Medicine and Toxicology Faculty of Medicine - Ain Shams University

Prof. Dr. Seham F. Abd Ell-All

Prof. of Forensic Medicine and Toxicology Faculty of Medicine - Ain Shams University

Dr. Sahar Saad El-Din Zaki

Ass. Prof. of Pathology Faculty of Medicine - Ain Shams University

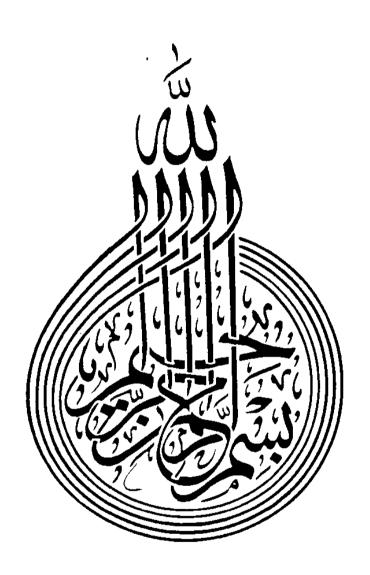
Dr. Asmaa Ahmed Fawzy Assaf

Lecturer of Forensic Medicine and Toxicology Faculty of Medicine - Ain Shams University

> Faculty of Medicine Ain Shams University

> > 1996





## **ACKNOWLEDGMENT**

I would like to extend my thanks and appreciation to Prof. Dr. Ahmed Kamel Mashhour, Head of Department of Forensic Medicine and Toxicology, Faculty of Medicine, Ain Shams university, for his contineous help and encouragement all through the work.

I would like to express my sincerest gratitude to **Prof. Dr. Naila Ahmed El-Nayal, Prof. of Forensic Medicine and Toxicology, Faculty of Medicine, Ain Shams University** for her great support and co-operation, valuable guidance. It is a great honour to work under her supervision.

I wish to express my heartful thanks to Prof. Dr. Seham Fouad Abd El All, Prof. of Forensic Medicine and Toxicology, Faculty of Medicine, Ain Shams University for her continuous invaluable advises. She kindly directed me and offered fer precious time generous care to accomplish this thesis in a proper time.

I am so obliged to Dr. Sahar Saad El Din Zaki, Ass. Prof. of Pathology, Faculty of Medicine, Ain Shams University for her efforts in reading and interpreting the pathological sections. She was kind and helpful.



My sincere thanks to Dr. Asmaa Ahmed Fawzy Assaf, Lecturer of Clinical Toxicology, Faculty of Medicine, Ain Shams University for her honest and great support all through the work.

Many thanks to Dr. Mervat Hassan Abdul-Aziz, Lecturer of Community Medicine, Faculty of Medicine, Ain Shams University for her kind help in the statistical analysis of the data of this work.

Einas Aboul-Wafa



## **DEDICATION**

- ▼ TO MY LATE FATHER WHO WISHED TO SEE THIS WORK COMPLETED BEFORE HE PASSED AWAY
  - **▼ TO MY HUSBAND** 
    - **▼ TO MY FAMILY**

### **CONTENTS**

INTRODUCTION	1
AIM OF THE WORK	2
REVIEW OF LITERATURE	
Methotrexate	3
Tolmetin and ketoprofen	24
METHODOLOGY	47
RESULTS	59
DISCUSSION	140
RECOMMENDATIONS	150
SUMMARY	151
REFERENCES	153
ARABIC SUMMARY	



#### **ABBREVIATIONS**

**7-OH MTX**: 7-hydroxy methotrexate

ALP: Alkaline phosphatase

ALT: Alanine aminotransferase

AST: Aspartate aminotransferase

**DHFR**: Dihydrofolate reductase

Hb conc.: Haemoglobin concentration

HCO<sub>3</sub>: Bicarbonate level

IM: Intramuscular

IP: Intraperitoneal

IV: Intravenous

MTX: Methotrexate

NSAIDs: Non-steroidal antiinflammatory drugs

**PGs**: Prostaglandins

Plat. Count: Platelet count

RBCs: Red Blood cell count

TLC: Total leucocytic count

