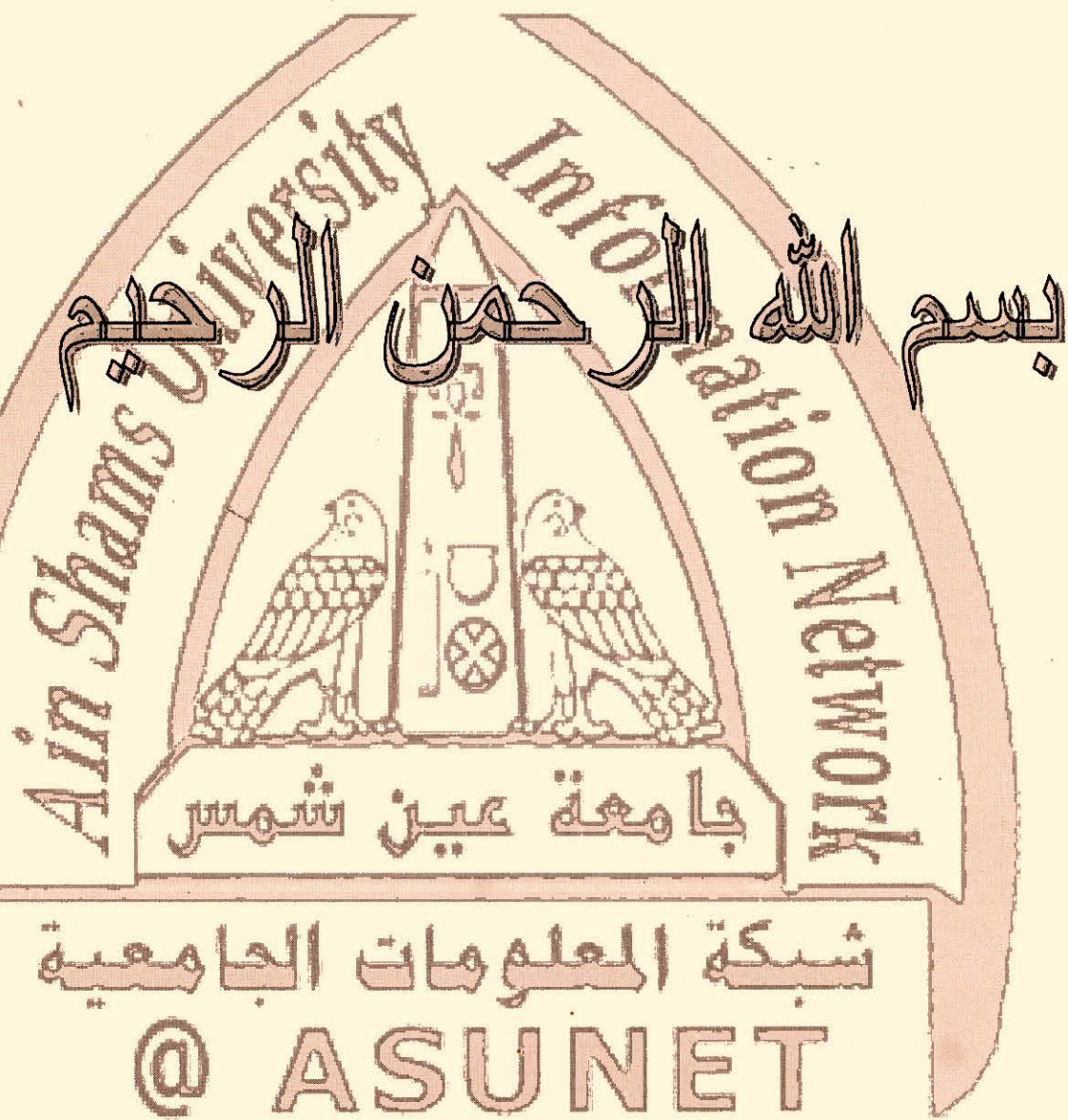




شبكة المعلومات الجامعية





شبكة المعلومات الجامعية

# جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

## قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها  
علي هذه الأفلام قد أعدت دون أية تغيرات



## يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من ١٥-٢٥ مئوية ورطوبة نسبية من ٢٠-٤٠%

To be Kept away from Dust in Dry Cool place of  
15-25- c and relative humidity 20-40%





# شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



# بعض الوثائق الأصلية تالفة



# بالرسالة صفحات لم ترد بالأصل

**A STUDY ON GLUCURONIDE, SULFATE  
AND GLUTATHIONE SYSTEMS  
IN BLADDER CANCER TISSUES**

615.19

**Thesis**

**Submitted to**

**Medical Research Institute**

**Alexandria University**

**In**

**Partial Fulfillment of the requirements of the**

**Degree**

**Of Master Applied Medical Chemistry**

---

**By**

**Rania Mohammed El Lethy**

**B.Sc. Chemistry-Faculty of Science-Menoufiya University 1996**

**Medical Research Institute**

**Alexandria University**

**2005**

C.R. - R  
C.D.



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ تَوَدُّ أَنْ يُسْجَدَ لَكَ فَسَبِّحْ لِلَّهِ مَا تَشَاءُ  
لَا يُلَاقِيكَ فِيهَا مِنْ حَسْبٍ وَمَنْ يَفْعَلْ ذَلِكَ  
بِغَيْرِ إِيمَانٍ فَهُوَ مُجْرِمٌ وَالَّذِينَ آمَنُوا  
وَعَمِلُوا الصَّالِحَاتِ لَهُمْ أَجْرٌ كَثِيرٌ  
وَلَا يُلَاقِيكَ فِيهَا مِنْ حَسْبٍ وَمَنْ يَفْعَلْ ذَلِكَ  
بِغَيْرِ إِيمَانٍ فَهُوَ مُجْرِمٌ وَالَّذِينَ آمَنُوا  
وَعَمِلُوا الصَّالِحَاتِ لَهُمْ أَجْرٌ كَثِيرٌ

صدق الله العظيم

سورة البقرة آية ٢٢

# **Supervisor**

**Prof. Dr. Shehata Mahmoud El-Sewedy**  
Professor of Applied Medical Chemistry  
Applied Medical Chemistry Department  
Medical Research Institute  
Alexandria University

**Prof. Dr. Tousson Abul-Azm**  
Professor of Urology  
Urology Department  
Faculty of Medicine  
Alexandria University.

**Dr. Mohammed Ahmed Abdel-Mohsen**  
Lecturer of Applied Medical Chemistry  
Applied Medical Chemistry Department  
Medical Research Institute  
Alexandria University

**Dr. Amal Sobhy Mahmoud El-Sedfy**  
Lecturer of Pathology  
Pathology Department  
Medical Research Institute  
Alexandria University



تم مناقشة الرسالة علانياً بمعهد البحوث الطبية يوم الخميس الموافق ٢٠٠٥/٦/٣٠ م  
وتم قبول الرسالة بدرجة ٣٠٪ بتقدير جيد... وتم عمل التعديلات اللازمة

شحاته السويدي

رئيس لجنة الحكم

أ.د/ شحاته محمود السويدي

رئيس القسم

أ.د. نبيل جابر

(أ.د. نبيل جابر على حاشية)

# Acknowledgment

Thank to Allah who enabled me completing this thesis.

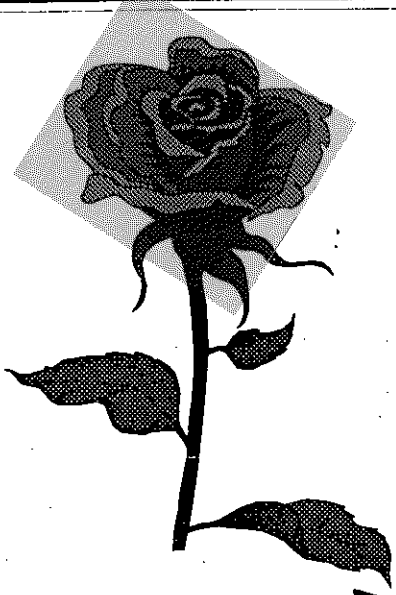
It is great pleasure to express my deepest gratitude to Prof. Dr. **Shehata Mahmoud El-Sewedy**. Professor of Applied Medical chemistry, Medical Research Institute, Alexandria University. Who patiently devoted much of his precious time and effort to give me helpful advice and excellent supervision, and for his kind encouragement, continuous support and great help for the facilitation of all difficulties to accomplish this work.

I would like to express my gratitude and cordial appreciation to prof. Dr. **Tousson Abul-Azm**, professor of Urology, Faculty of Medicine, Alexandria University, for his kind help in managing and supplying the information of all cases.

I am great indebted to Dr. **Mohammed Ahmed Abdel-Mohsen**, Lecturer of Applied Medical Chemistry, Medical Research Institute. Alexandria university. For his help, encouragement and supervising during the whole work; Without this keen supervision, this work will never have been completed.

I am also depply indebted to Dr. **Amal Sabhy Mahmoud El-Sedfy**, Lecturer of pathology, pathology Department, Medical Research Institute, Alexandria University, for her help guidance in the histopathological and immunohistochemical assessment in this work.

I also thanks to all staff members of Applied Medical Chemistry, Medical Research Institute, Alexandria University, for their kind cooperation during the whole work.



# Dedicated to

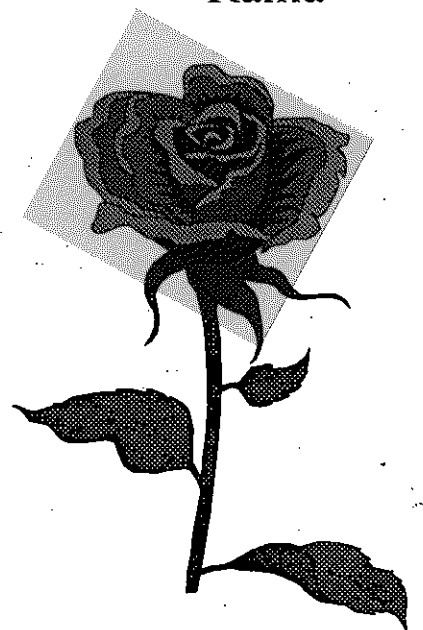
My Mother,

My Husband,

My son,

And to all my family,

Rania





# Contentes:

• Introduction .....	1
<b>I. Epidemiology of urinary bladder cancer.</b> .....	<b>1</b>
<b>II. Etiology of urinary bladder cancer.</b> .....	<b>2</b>
1. Smoking. ....	2
2. Bacterial infection. ....	3
3. Bladder stones. ....	4
4. Schistosomes. ....	4
5. Occupational exposure. ....	6
<b>III. Urinary bladder cancer related chemical carcinogens.</b> .....	<b>7</b>
a. Aromatic Amines .....	7
b. N-Nitroso compounds (NOC). ....	10
<b>IV. Biotransformation of chemical carcinogens.</b> .....	<b>13</b>
1. Glucuronide system. ....	15
a. uridine Diphospho Glucuronosyl transferase (UDPGT). ....	16
b. $\beta$ -Glucuronidase ( $\beta$ -Glase) .....	18
2. Sulfate system. ....	22
a. sulfotransferase (ST). ....	22
b. Arylsulfatase A (ASA). ....	25
3. Glutathione and Glutathione-S-transferase. ....	27

a. Glutathione (GSH).-----	27
b. Glutathione –S- transferase (GSTS).-----	31
• Aim of the work.-----	34
• Material and Methods.-----	35
* Material.-----	35
1. chemicals.-----	35
2. Subjects.-----	35
3. Tissue samples.-----	35
Pathological studies.-----	37
Biochemical studies.-----	39
1. Determination of uridinediphosphoglucurolosyl transferase activity (UDPGT).-----	39
2. Determination of $\beta$ -Glucuronidase activity ( $\beta$ -Glase).-----	41
3. Determination of phenal sulfotransferase activity (ST).-----	43
4. Determination of Arylsulfatase A activity (ASA).-----	45
5. Determination of Reduced Glutathione GSH content.-----	47
6. Determination of Gluathione –S- transferase activity (GST).---	48
7. Determination of protein content.-----	50
• Results.-----	52
I. Histopathological Results.-----	55
II. Biochemical Results.-----	59
1. UDP-glucuronosyl transferase (UDPGT)-----	59

2.	<b>β-Glucuronidase (β-Glase)</b> .....	62
3.	<b>Sulfotransferase (ST)</b> .....	65
4.	<b>Arylsulfatase A (ASA)</b> .....	68
5.	<b>Glutathione content (GSH)</b> .....	71
6.	<b>Glutathione –S- transferase (GST)</b> .....	74
	<b>Level of conjugation / deconjugation of glucuronide and sulfate system</b> .....	77
	<b>Symbolic summary for the biochemical results</b> .....	78
	<b>Appendix from 1 to 7</b> .....	79
<b>III.</b>	<b>Biostatistical correlation.</b> .....	85
	• <b>Discussion</b> .....	86
	• <b>Summary and conclusions</b> .....	98
	• <b>Reference</b> .....	102



## LIST OF ABBREVIATIONS

AAAF	N-Acetoxy-2-acetylaminofluorene
AAF	2-Acetyl amino fluorene
OAT	O-Acetylation
RN <sup>+</sup> Ac	Acetyl nitroenium ion
NAT	N-acetyltransferase
N,O-AT	N,O-Acetyltransfer
4-ABP	Aminobiphenyl
MeIQ	2-amino-3,4-dimethylimidazo[4.5-f] quinoline
ADP	Adenosine diphosphate
ATP	Adenosine triphosphate
APS	Adenosyl 1-5'-phosphosulphate
AAs	Aromatic amines
ASA	Arylsulfatase
AST	Aryl Sulfotransferase
CDNB	1-chloro-2,4-dinitrobenzene
cDNA	complementary DNA
DNA	Deoxyribonucleic acid
DMSO	Dimethyl sulfoxide
DTNB	5,5'-dithiobis-2-nitrobenzoic acid
EDTA	Ethylene diamine tetracetic acid
$\beta$ -Glase	$\beta$ -Glucuronidase
GSH	Glutathione
GST	Glutathione-S-transferase
ISUP	International society of urological pathologists
NAD <sup>+</sup>	Nicotinamide adenine dinucleotide (oxidized)
NADH	Nicotinamide adenine dinucleotide (Reduced)
RN <sup>+</sup> H	Nitrenium ion
NAs	N-Nitrosamines
NOC	N-Nitroso Compounds
PhIP	Phenylimidazo pyridine
PAPS	3-Phosphoadenosyl 1-5'-phosphosulfate
PAHs	polycyclic aromatic hydrocarbons
PPi	Pyrophosphate inorganic
RNA	Ribonucleic acid
NaOH	Sodium hydroxide