



Biochemical studies on active metabolites of sponge-and coral-associated fungi *in-vivo* and *in-vitro*

A thesis Submitted for the fulfillment of Ph.D. degree in biochemistry

Presented by

Zeinab Abd El-Khalek Ali El-Shahid

Assistant Researcher at National Research Centre

M.Sc. in Biochemistry

(2005)

Under Supervision of

Dr/Eman M. Abd-El Azeem

Professor of Biochemistry

Biochemistry Department

Faculty of Science

Ain Shams University

Prof/Faten K.Abd El-Hady

Professor of Natural Product Chemistry

Natural and microbial Product

Chemistry Department

Pharmaceutical Industry and Drug

Research Division

National Research Centre

Dr/Emad Khairy Ibrahim Ahmed

Assistant Professor of Biochemistry

Biochemistry Department

Faculty of Science

Ain Shams University

2018

Ain Shams University
Faculty of Science
Department of Biochemistry



**Biochemical studies on active
metabolites of sponge-and coral-
associated fungi *in-vivo* and *in-vitro***

Submitted by

Zeinab Abd El-Khalek Ali El-Shahid

Assistant Researcher at National Research Centre
M.Sc. in Biochemistry(2005)
For Fulfillment of PhD Degree in Biochemistry

Under Supervision of

Faten K. Abd El-Hady

Prof Dr.Eman M. Abd-El Azeem

Professor of Biochemistry
Biochemistry Department
Faculty of Science
Ain Shams University

Prof Dr.Faten K.Abd El-Hady

Professor of Natural Product Chemistry
Natural and Microbial Product
Chemistry Dept.
Pharmaceutical Industry and Drug
Research Division
National Research Centre

Dr/Emad Khairy Ibrahim Ahmed

Assistant Professor of Biochemistry
Biochemistry Department
Faculty of Science
Ain Shams University

Emad D. Ahmed

2018

Department of Biochemistry
Faculty of Science
Ain Shams University



{ **تَمَانِي فِي** **الْإِسْلَامِ** **عَلَيْهِ تَوَكَّلْتُ وَإِلَيْهِ أُنِيبُ** }

@PEARLA0203

Declaration

I declare that this thesis has been composed by me and the work and data that has been recorded in this thesis was done by me.

This thesis has not been submitted for a degree in any other universities.

Biography

Name:	Zeinab Abd El-Khalek Ali Elshahid.
Faculty	Faculty of Science, Helwan University, Chemistry/Biochemistry Department, very Good, 1999.
Degree awarded	M.Sc. of Biochemistry, Chemistry/Biochemistry Department, Faculty of Science, Helwan University, 2005.
Date of registration	12-10-2015.
Grade	Ph.D in Biochemistry.
Current Position	Research Associate.
Work	Chemistry of Natural and Microbial Products Department, Pharmaceutical Industry and Drug Research Division, National Research Center.



Dedicated to.....

My beloved Father,

My Great Mother,

My Dear Husband

My lovely sweet daughters,

My Wonderful Brothers,



Acknowledgment

In the Name of Allah, Most Gracious, Most Merciful

I do thank Allah, He's given me the Courage and strength to complete this work and he's benefited me with those, most respectable and efficient supervisors.

I'm very much honored to have ***Prof. Dr. Eman M. Abdel Azeem***, Professor of Biochemistry, Faculty of Science, Ain Shams University, supervise this work, sincere guidance and continuous support. No words are sufficient to express heart felt, thanks to her

I would like to express my deepest thanks and gratitude to ***Prof. Dr. Faten Kamal Abd El Hady***, Professor of Natural Product Chemistry, National Research Center, for her Patience, generous help, sincere guidance and continuous supervision and encouragement during the entire work.

I would like also to express my deepest thanks and gratitude to ***Dr. Emad Khairy Ibrahim Ahmed***, assistant Professor of Biochemistry, Faculty of Science, Ain Shams University, for his patience, help and continuous advices .

I'm deeply and greatly indebted to ***Prof. Dr. Mohamed S. Abdel-Aziz***, Professor of Microbiology, Microbial Chemistry Department, National Research Center, for his supervision sincere guidance and continuous support. I'm honored having him as an eminent member of the supervision board.

I wish to express my sincere appreciation and infinite gratitude to ***Dr. Walid M. Fayad***, associate Professor of pharmacognosy, Drug Bioassay-Cell Culture Laboratory, National Research Center, for his continuous support , help and guidance to fulfill this entire work .



Sincere thanks to Dr. Hassan Darwish , cell biology department, for his kind help and support .

Sincere thanks and gratitude to all members of Pharmacognosy department, prof. dr. *Khaled Mahmoud* ; dr. *Ahmed Abd El-fattah*, dr. *May Aly El-Manawaty* ; dr. *Salwa El-Hallouty* ; for their kind help , support and encouragement throughout the entire work .

Sincere thanks and deepest gratitude to all my friends and colleges in chemistry of natural product Lab; dr. Nesma M. Salah, dr. Eman A. Ali, dr. Amal Mosaad and my late colleague: dr. Laila S. Ibraheem (RIP).

Sincere thanks and deepest gratitude to Prof. Dr. Heba A. Elrefaai and Prof. Dr. Mona Shafei, for their great support.

Sincere thanks and deepest gratitude to all my friends and colleges in Pharmaceutical and Drug Industries Research Division and to everyone that helped me to accomplish this work.

Last, but not least, My deepest gratitude and love to all my family, my Mom , My Dad, my lovely daughters, my husband, my brothers , my sisters in law and special thanks to dr. Nancy Aziz, my sister in law.

Subject	Page no.
List of Tables	
List of figures	
List of abbreviations	
Abstract	I-II
Indroduction	1-3
Aim of the work	4
Review	5-36
<i>1-Bioprospecting</i>	
<i>2-Marine systems as a source of natural bioactive compounds</i> <i>2.1. History of Marine Natural Products</i> <i>2.2.Sources of Marine Natural Products (MNPs)</i> 2.2.1Marine sponge 2.2.2. Marine Soft Coral 2.2.3.Marine fungi 2.2.3.1.Fungi associate relationships as a source of bioactive compound 2.2.3.2Aspergillus sp	11
<i>2.3. Red sea a rich source of biodiversity and chemodiversity</i>	
<i>2.4. Chemical diversity of marine bioactive secondary metabolites:</i> <i>2.4.1Terpenes</i> <i>2.4.2.Peptides</i> <i>2.4.3. Alkaloids</i> <i>2.4.4. Polyketides</i> <i>2.4.5. Polysaccharide</i>	
<i>2.5. Marine fungal products in therapeutic use</i> <i>2.5.1. Cytotoxic natural products in therapeutic use</i> <i>2.5.2 Cytotoxic fungal metabolites from the marine habitat</i>	
<i>3. Red sea microorganisms (fungi) isolation</i> <i>3.1. Activation of Silent Gene Clusters for New Fungal Secondary Metabolites</i> <i>3.2 Extraction of bioactive compounds: overview of sample preparation and extraction conditions</i>	
<i>4 .Overview of bioactive metabolites screening</i> <i>4.1. The biological significance of marine fungal secondary metabolites</i> <i>4.1.1.Antibacterial activity</i>	