شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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Cairo University
Faculty of science
Chemistry Depart.

Molecular Genetic and Cytotoxic Evaluation of Novel Synthesized Hybrid Steroid Derivatives as Chemotherapeutic Anti-Breast Cancer Agents

Presented by

Ghada Hamdi Elsayed Mohammad

A Thesis Submitted to
Faculty of Science

In Partial Fulfillment of the
Requirements for the Degree of
Master of Science (Organic Chemistry)

Chemistry Department
Faculty of Science
Cairo University

2010-2011

APROVAL SHEET FOR SUMISSION

Thesis Title: **Molecular Genetic and Cytotoxic Evaluation of Novel Synthesized Hybrid Steroid Derivatives as Chemotherapeutic Anti-breast Cancer Agents.**

Name of candidate: Ghada Hamdi Elsayed Mohammad

This thesis has been approved for submission by the supervisors:

1- Prof. Dr: Rafat Milad Mohareb

Signature:

2- Prof. Dr: Hussein Fouad Zohdi

Signature:

3- Ass. Prof. Dr: Gamal Abd Elmegeed Abd Elghany

Signature:

Prof. Dr. Mohamed Badawy
Chairman of Chemistry Department
Faculty of Science- Cairo University

Chairman of Chemistry Department
Faculty of Science, Cairo University

Addendum

Beside the work carried out in this thesis, the candidate ***Ghada Hamdi Elsayed Mohammad*** has attended Post-graduate courses during the academic year 2006-2007 in the following topics:

- Biochemistry
- New Trends in Analytical Chemistry
- Carbohydrate Chemistry
- Chemistry of Natural Products
- Designing Organic Chemistry
- Applied Organic Chemistry
- Organic Photochemistry
- Polymer Chemistry
- Quantum Chemistry
- Organic Microanalysis
- Heterocyclic Chemistry
- Techniques of Molecular Structure Determination
- German language
- Selected Topics

She has also passed successfully an examination in the above mentioned topics.

Prof. Dr. Mohamed Badawy

Chairman of Chemistry Dept.
Faculty of Science, Cairo University.

ABSTRACT

Student Name: Ghada Hamdi Elsayed Mohammad

Title of the thesis: Molecular Genetic and Cytotoxic Evaluation of Novel Synthesized Hybrid Steroid Derivatives as Chemotherapeutic Anti-Breast Cancer Agents.

Degree: M. Sc. **Specialist: Organic Chemistry**

Hybrid anti-cancer agents, which combine two biologically active compounds in one such as steroidal heterocyclic derivatives attain both hormone and cytotoxic effects on cancer cells. The aim of the present study is to synthesize and evaluate new potential hybrid chemotherapeutic anti-breast cancer agents. Several pyridazino-, pyrimido-, quinazolo-, oxirano- and thiazolo steroid derivatives were synthesized using 3β-hydroxy-5α-androstan-17-one (epi-androsterone) **1** as starting steroid. The structure of the novel steroid derivatives was confirmed using the analytical and spectral data. The most structurally promising of the novel synthesized hybrid steroids, compounds **8, 12, 17, 20, 22c, 24c, 30a** and **30b,** were investigated individually as anti-breast cancer agents against the human breast cancer cells (MCF-7) using SRB assay. The tested compounds **17, 20, 22c** and **8** showed promising broad spectrum cytotoxic activity *in vitro* after 48 hour incubation. Compound **17** (IC_{50} = 2.5μM) exhibited more inhibition effect of MCF-7 growth than Dox (IC_{50} = 4.5μM) after 48 h incubation time. The results of the present study showed that all the tested hybrid steroid derivatives showed significant decrease with various intensities in gene expression of breast cancer related genes (VEGF, CYP19, hAP-2γ and hAP-2α). Compounds **17, 20** and **22c** were the more effective in this respect.

Keywords: Breast cancer, Cytotoxicity, Gene expression, Heterocycles, Steroids.

Supervisors: **Signature:**

1- Prof. Dr: Rafat Milad Mohareb

2- Prof. Dr: Hussein Fouad Zohdi

3- Ass. Prof. Dr: Gamal Abd Elmegeed Abd Elghany

Prof. Dr. Mohamed Badoy
Chairman of Chemistry Department
Faculty of Science- Cairo University

بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

(البقرة:32)

صدق الله العظيم

Dedication

I dedicate this work

To

My Parents

Acknowledgement

I wish to express my deepest and sincere appreciation to ***Prof. Rafat M Mohareb****, Professor of Organic Chemistry, Chemistry Department, Faculty of Science, Cairo University, for suggesting the chemistry idea, kindly supervising the present work, reading and criticizing the Thesis.*

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Ghada Hamdi Elsayed

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