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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

م.م.ع.د

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)**

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Faculty of Science
Cairo University**

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APPROVAL SHEET FOR SUMISSION

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

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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:

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- 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

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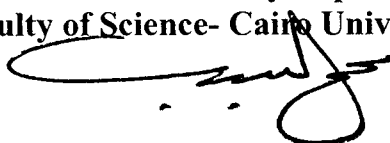
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ABSTRACT**Student Name: Ghada Hamdi Elsayed Mohammad****Title of the thesis: Molecular Genetic and Cytotoxic Evaluation of Novel Synthesized Hybrid Steroid Derivatives as Chemotherapeutic Anti-Breast Cancer Agents.****Degree: M. Sc. Specialist: Organic 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-5 α -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** ($IC_{50} = 2.5\mu M$) exhibited more inhibition effect of MCF-7 growth than Dox ($IC_{50} = 4.5\mu M$) 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-2 γ and hAP-2 α). Compounds **17**, **20** and **22c** were the more effective in this respect.

Keywords: Breast cancer, Cytotoxicity, Gene expression, Heterocycles, Steroids.**Supervisors:****1- Prof. Dr: Rafat Milad Mohareb****2- Prof. Dr: Hussein Fouad Zohdi****3- Ass. Prof. Dr: Gamal Abd Elmegeed Abd Elghany****Signature:**

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

اللَّهُمَّ صَلِّ عَلَى سَيِّدِنَا مُحَمَّدٍ إِنَّكَ أَنْتَ الْعَلِيمُ الْعَظِيمُ

(البقرة: 32)

صَدَقَ اللَّهُ الْعَظِيمُ

Dedication
I dedicate this work
To
My Parents

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