**Faculty of Science**
**Chemistry Department**

# "Synthesis and evaluation of some surface active agents based on Michael addition reaction and their application in some vital fields"

***A Thesis Submitted for Degree of Ph.D. in Chemistry***

*By*

***Fatma Mahmoud Abd Elhafiz Ahmed***

(M.Sc. Organic Chemistry)

*To*

**Chemistry Department, Faculty of Science**

**Ain Shams University, *Cairo, Egypt***

*Supervised by*

**Prof. Dr. Elsayed A. Soliman**
Prof. of Organic Chemistry
Chemistry Department, Faculty of Science, Ain Shams University

**Prof. Dr. Tawfik M. Kassem**
Prof. of Applied Organic Chemistry
Petrochemicals Department,
Egyptian Petroleum Research Institute

**Prof. Dr. Ammona S. Mohamed**
Prof. of Applied Organic Chemistry
Petrochemicals Department
Egyptian Petroleum Research Institute

**Assoc. Prof. Dalia E. Mohamed**
Assoc. Prof. of Organic Chemistry
Petrochemicals Department
Egyptian Petroleum Research Institute

**2018**

**Faculty of Science**
**Chemistry Department**

# "Synthesis and evaluation of some surface active agents based on Michael addition reaction and their application in some vital fields"

***A Thesis Submitted for Degree of Ph.D. in Organic Chemistry***

*By*

***Fatma Mahmoud Abd Elhafiz Ahmed***
(M.Sc. Organic Chemistry)

*To*

Chemistry Department, Faculty of Science
Ain Shams University, *Cairo, Egypt*

*Supervised by*

**Prof. Dr. Elsayed A. Soliman**
Prof. of Organic Chemistry
Chemistry Department, Faculty of Science, Ain Shams University

**Prof. Dr. Tawfik M. Kassem**
Prof. of Applied Organic Chemistry
Petrochemicals Department,
Egyptian Petroleum Research Institute

**Prof. Dr. Ammona S. Mohamed**
Prof. of Applied Organic Chemistry
Petrochemicals Department
Egyptian Petroleum Research Institute

**Assoc. Prof. Dalia E. Mohamed**
Assoc. Prof. of Organic Chemistry
Petrochemicals Department
Egyptian Petroleum Research Institute

**Head of Chemistry Department**

**Prof. Dr. Ebrahim Hosani Ali Badr**

**2018**

**Ain Shams University**
**Faculty of Science**
**Chemistry department**

## Approval Sheet

**Student Name:** *Fatma Mahmoud Abdelhafiz Ahmed "M.Sc in organic Chemistry"*

**Thesis Title:** *"Synthesis and evaluation of some surface active agents based on Michael addition reaction and their application in some vital fields".*

**Supervisors Committee:** **Signature**

1- **Prof. Dr. Elsayed A. A. Hegazy**
Prof. of Radiation Chemistry
National Center for Radiation Research
and Technology, Atomic Energy Authority

2- **Prof. Dr. Nehal O. Shaker**
Prof. of Applied Organic Chemistry
Faculty of Science, Al- Azhar University (Girls)

3- **Prof. Dr. Prof. Dr. Elsayed A. Soliman**
Prof. of Organic Chemistry
Chemistry Department, Faculty of Science
Ain Shams University

4- **Prof. Dr. Tawfik M. Kassem**
Prof. of Applied Organic Chemistry
Petrochemicals Department,
Egyptian Petroleum Research Institute

**Head of Chemistry Department**
**Prof. Dr. Ebrahim H. A. Badr**

# QUALIFICATION

**Name** **:** Fatma Mahmoud Abd Elhafiz

**Science Degree** **:** M.Sc.

**Department** **:** Chemistry

**College** **:** Faculty of Science

**University** **:** Benha University

**M.Sc** **:** 2013

# *Acknowledgement*

*First, I would like to thank "**Allah**" for giving me the opportunity and the strength to accomplish this work.*

*I would like to express my deepest gratitude, appreciation and respect to:*

***Prof. Dr. Elsayed A. soliman,** Professor of Organic Chemistry, Chemistry Department, Faculty of science, Ain Shams University. for his continuous valuable supervision, ongoing assistance and advice throughout this work.*

***Prof. Dr. Tawfik M. Kassem,** Professor of Applied Organic Chemistry, Egyptian Petroleum Research Institute (EPRI), for his direct supervision, valuable discussions and continuous encouragement during all phases of this work.*

***Prof. Dr. Ammona S. Mohamed,** Professor of Applied Organic Chemistry, Egyptian Petroleum Research Institute, for her guidance in suggesting the research point; valuable assistance, guidance in the experimental work. I am grateful for the time and efforts taken by her to read and correct the written materials, presenting the thesis in its final form and for her gentle treatment.*

***Dr. Dalia E. Mohamed***, *Associate Professor, Egyptian Petroleum Research Institute, for her advices, supervision, valuable discussions, guidance in the experimental work. I am grateful for the time and efforts taken by her to read and correct the written materials and for her gentle treatment.*

***Dr. Abeer Mostafa Khattab,*** *researcher, National Organization for Drug Control and Research, for her valuable cooperation in performing the experimental work of the drug delivery part as well as her valuable sharing in writing this part. I am grateful for her advices and valuable discussions.*

*Finally, I would like to thank* ***my colleagues*** *and all members of Petrochemicals Department, (EPRI) Egyptian Petroleum Research Institute, especially Surface Active Agents Lab., for providing the facilities to carry out the practical work.*

# DEDICATION

*To My PARENTS*

***I have to thank Allah for choosing both of you to be my parents.***

***Thank you for supporting me***

*TO MY DEAR HUSBAND,*

*MY DEAR DAUGHTERS*

*AND SON*

*TO MY FAMILY*

**Thank you for supporting and helping me**

# Aim of the work

This work aimed to prepare different surface active agent compounds in the form of dendrimers with different generations based on Michael addition reaction, elucidate their chemical structures, evaluate their surface activity and finally, apply them in different vital fields. So, the main target of this thesis can be summarized as follows:

1- **Synthesis** of different generations of polyamidoamine (PAMAM) cationic surfactants using piperazine as core center molecule and ethylene diamine as a repeated unit. This synthesis produced generations of different dendrimer surfactants terminated with methyl ester PAMAM-$COOCH_3$ and amine PAMAM-$NH_2$ end groups.

2- **Confirmation** of the chemical structures of the synthesized compounds using FTIR, $^1$H-NMR and Elemental analysis.

3- **Evaluation** of the surface activity and thermodynamic parameters of the synthesized compounds using surface tension technique at 25$^o$C.

4- **Application** of the synthesized dendrimer surfactants in different vital fields:

## 4.1- Biological Applications:

**a- Antimicrobial activity:** Evaluation of all the synthesized polyamidoamine cationic surfactants as biocides against different pathogenic bacterial and fungal species.

**b- SRB:** Evaluation of some selected PAMAM-$COOCH_3$ and PAMAM-NH2 compounds against sulfate reducing bacteria.

**c- Anti-tumor Agents:** Evaluation of all the synthesized polyamidoamine cationic surfactants as anti-tumor agents against breast cancer cell.

## 4.2- Drug Delivery Applications

**a- Solubility Study of a Hydrophobic Drug** using the synthesized polyamidoamine cationic surfactants as solubilizing agent for a poorly soluble drug (coenzyme Q10).

**b- Dissolution Study** selection of the compounds that gave the highest solubility value to be evaluated in dissolution study of both coenzyme Q10 and Ledipasvir drug.

**c- The toxicity test:** Evaluating the toxicity of two of the prepared compounds.

# Abstract

**Title:** "Synthesis and evaluation of some surface active agents based on Michael addition reaction and their application in some vital fields".

***By***

***Fatma Mahmoud Abd Elhafiz Ahmed***

Chemistry Department, Faculty of Science, Ain Shams University

**Degree:** Doctor of Philosophy in Organic Chemistry,

Faculty of Science, Ain Shams University, 2018.

Different generations of cationic hyperbranched polyamidoamine (PAMAM) quaternary ammonium salt dendrimers terminated with methyl ester and amine end groups were synthesized. Preparation of these dendrimers was carried out via alternative steps of aza Michael addition reaction (of piperazine as core center molecule) and amidation reaction (by ethylene diamine). Each step was followed by quaternization using alkyl bromide with different chain length (4, 8 or 12) carbon atoms. The chemical structures of the prepared dendrimers were confirmed using FTIR, $^{1}$H-NMR spectra and elemental analysis. Also their surface activity has been studied and their surface parameters including surface and interfacial tension, emulsification power, critical micelle

concentration, effectiveness, efficiency, maximum surface excess and minimum surface area were determined. The prepared quaternized dendrimers were applied in different fields where most of them revealed significant results. First, the dendrimers were tested as antimicrobial agents against different strains of bacteria, yeast and fungi, where the results showed that they have significant results as antimicrobial agents. Then, the compounds which gave the most significant biocidal activity were selected to be evaluated against sulfate reducing bacteria. Also, the synthesized polyamidoamine cationic surfactants were applied as anti-tumor agents against breast cancer cell, in which they showed good activity. Finally, in the field of drug delivery, all the synthesized polyamidoamine cationic surfactants were used as solubilizing agents for a poorly soluble drug (coenzyme Q10). The compounds that gave the highest solubility value were selected to be evaluated in the dissolution study of both coenzyme Q10 and Ledipasvir drug. Finally, the toxicity test was performed for two selected compounds from the prepared dendrimers and the results proved safety of these compounds.

**Key words:** Piperazine; ethylene diamine; Michael addition reaction; hyperbranched polyamidoamine, antimicrobial agents, anticancer and drug delivery.

# *LIST of CONTENTS*