

Dr. Maria Koufaki

Senior Researcher

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EDUCATION

Ph.D. 1988, University of Geneva, Pharmacy Department, Switzerland "Desoxyhydroxyaminosucres par cyclisation ou reduction des nitrones et radicaux libres correspondants. Nouvelles voies de synthese d'oligosaccharides"

B.S. 1983, (in Chemistry) National University of Athens, Greece.

EMPLOYMENT

1983-1988 Teaching Assistant University of Geneva, Switzerland.

1989-2002 Researcher at the Institute of Organic and Pharmaceutical Chemistry of the National Hellenic Research Foundation, (IOPC/NHRF) Athens.

2002- Senior Researcher at the Institute of Organic and Pharmaceutical Chemistry of the National Hellenic Research Foundation, (IOPC/NHRF) Athens

FELLOWSHIPS

8/1986 Societ  Acad mique de Gen ve

7-12/ 1991 Fulbright Research Award, University of Connecticut

FOREIGN LANGUAGES

French (excellent), English (excellent), German (working knowledge).

RESEARCH EXPERIENCE

Research interests are focused on the design and synthesis of molecules with pharmacological activity.

In particular:

a) Ether lipids that either possess anticancer or antileishmanial activity or act as carriers for widely used anticancer or anti-HIV agents in order to achieve improved delivery and targeting

b) Bifunctional agents possessing antioxidant and antiarrhythmic activity

c) Chroman/1,2 dithiolane hybrids possessing cardioprotective and neuroprotective activity

d) Chroman/catechol hybrids and iron chelators active against glutamate neurotoxicity and oxidative stress induced cellular DNA damage.

Research experience includes design and synthesis of spin labeled heterocyclic compounds such as carbohydrates and nucleosides.

FUNDING

NDO (EOF) (1991-94) "Design and Synthesis of alkyllysophospholipids"

KESY (1993-95). "Synthesis and biological activity of new tamoxifen analogues"

EKVAN 115 (1998-2000). "Peptide mimetics"
PENED 99 181 (2000-01) "Development of novel biochemical methods for the evaluation of compounds possessing antioxidant properties".
Excellence in the Research Institutes (2002-05) "Novel strategies against neurodegeneration"
COST D13/0019/01 (2001-04) "Novel molecules, Forms and Strategies for treatment of Leishmanial Infections"
Univ. Connecticut PSA No 2328 (1998-99) "Novel antiarrhythmics and anticancer ether lipids"
Univ. Connecticut PSA No 3324 (2001-02) "Biologically active ether phospholipids"
Univ. Connecticut PSA No 3680 (2002-03) "Novel Antioxidants"
Univ. Connecticut PSA No 4505 (2004-05) "Novel Antioxidants and Bioactive ether phospholipids"
GSRT programme Location and use of research results by the creation of new enterprises (Spin-off, 2003-05) "New ether phospholipids as ultrasound contrast agents"
Operational Programme for Competitiveness, GSRT YB/39 (2004-07). "Therapeutic Interventions Against Protozoan Infections".
Bilateral Collaboration of Greece-Hungary (2003-06). "Synthesis of novel antiarrhythmics and study of their electrophysiological effects".

CURRENT COLLABORATIONS

Prof. D. Galaris, Medical School, University of Ioannina Greece
 Ass. Prof. P. Papazafiri, Department of Biology, University of Athens
 Dr. M. N. Alexis, IBRB/NHRF
 Asc. Prof. A. Tsotinis, Pharmacy Department, University of Athens
 Asc. Prof. E. Iliodromitis, Medical School, University of Athens
 Dr. J. Andreadou, Pharmacy Department, University of Athens
 Prof. A Varro, Department of Pharmacology & Pharmacotherapy, University of Szeged, Hungary
 Prof. A. Makriyannis, Northeastern University, Boston, USA.

TEACHING EXPERIENCE

1983-1988 Teaching Assistant at the Department of Pharmaceutical Chemistry, University of Geneva, and trainer of technical personnel.
 1993-2004 Supervisor of 4 post-graduate and 1 post-doctoral fellows (IOPC)
 5/1998 Instructor in training seminar on "Modern Chemistry and its Applications" for chemistry teachers in secondary education in Greece.
 11/1999 Invited speaker at the post graduate program of the University of Athens School of Medicine. Title: "The role of free radicals in pathological conditions and specifically in myocardial ischemia-reperfusion".
 2001-2002 Co-supervisor of 3 diploma students (National Technical University Athens)
 2004 Supervisor of 1 post-graduate and 2 MSc fellows (IOPC).

OTHER ACTIVITIES

1993-1996 Member of the board Greek Chemical Society, Pharmaceutical Chemistry Division
 1996-1998 General secretary of the board Greek Chemical Society, Pharmaceutical Chemistry Division
 2004- Vice President of the board Greek Chemical Society, Organic and Pharmaceutical Chemistry Division
 1994-1998 Member of the board of Fulbright alumni
 1998-2000 Treasurer of the board of Fulbright alumni
 1993-2004 Member of the Organizing Committee of 11 Greek and 4 International Symposia
 2002-2003 Guest Editor of *Current Topics in Medicinal Chemistry* (Bentham Science Publishers Ltd. USA) Title of the issue: "Therapeutic strategies against HIV infection" (vol.3, no 13, 2003)
 2001- Reviewer of articles for the *Journal of Medicinal Chemistry* and *Bioorganic and Medicinal Chemistry*
 2005 Member of Editorial Advisory Board of *Current Topics in Medicinal Chemistry*

PUBLICATIONS

Tronchet J.M.J., Bizzozero N., **Koufaki M.**, Habashi F., Geoffroy M. Analogs of blocked disaccharides bearing a N-hydroxyimino bridge and nitroxyl free radicals thereof. *J. Chem. Research* **1989** (S) 334 and *J. Chem. Research* **1989** (M) 2601

Tronchet J.M.J., **Koufaki M.**, Zosimo-Ladolfo G. Spacer arms bearing two N- hydroxyimino groups and nitroxyl free radicals thereof. *Carbohydr. Res.* **1991**, 209 299-305

Tronchet J.M.J., **Koufaki M.**, Zosimo-Ladolfo G., Bernardinelli G. Spiro naphthoxazine derivatives of furanose sugars. *J. Chem. Research* **1992** (S) 293 and *J. Chem. Research* **1992** (M) 2501

Mavromoustakos T., Theodoropoulou E., **Koufaki M.**, Yang D.P. Lin S., Zervou M. Calogeropoulou T., Makriyannis A. Conformational analysis of 1-thiohexadecyl-2-O-methyl-*rac*-glycero-3-phosphocholine. *Epitheor Klin. Farmakol. Farmakokinet. Int. Ed.* **1993**, 11, 178

Mavromoustakos T., Theodoropoulou E., Polychroniou V., Dimitriou A., **Koufaki M.**, Calogeropoulou T. Study of drug membrane interactions using a combination of differential scanning calorimetry and ³¹P-NMR spectroscopy. *Epitheor Klin. Farmakol. Farmakokinet. Int. Ed.* **1995**, 13, 81.

Calogeropoulou T., **Koufaki M.**, Tsotinis A., Balzarini J., De Clercq E., Makriyannis A. Synthesis and anti-HIV evaluation of alkyl and alkoxyethyl phosphodiester AZT derivatives. *Antiv. Chem. Chemother.* **1995**, 6, 43-49

Koufaki M., Polychroniou V., Calogeropoulou T., Tsotinis A., Drees M., Fiebig H.H., LeClerc S., Hendriks H.R., Makriyannis. Alkyl and Alkoxyethyl Antineoplastic Phospholipids. *J. Med. Chem.* **1996**, 39, 2609-2614

Tsotinis A., Calogeropoulou T., **Koufaki M.**, Souli Ch., Balzarini J., De Clercq E., Makriyannis A. Synthesis and Antiretroviral Evaluation of New Alkoxy and Aryloxy Phosphate Derivatives of AZT. *J. Med. Chem.* **1996**, 39, 3418-3422

Koufaki M., Calogeropoulou T., Mavromoustakos T., Theodoropoulou E., Tsotinis A., Makriyannis A. Synthesis of ²H-Labelled Alkoxyethyl Phosphodiester AZT Derivatives for Solid-State ²H-NMR Studies. *J. Het. Chem.* **1996**, 33, 619-622

Mavromoustakos T., Theodoropoulou E., Yang D. P., Lin S. Y., **Koufaki M.**, Makriyannis A. The conformational properties of the antineoplastic ether lipid 1-thiohexyl-2-O-methyl-S-glycero-3-phosphocholine. *Chem. Phys. Lipids* **1996**, 84, 21-34

Tronchet J.M.J., **Koufaki M.**, Barbalat F., Geoffroy M. Blocked Sugar Analogues Bearing two or three N(sp³)-O Bonds. *Carbohydr. Lett.* **1999**, 3, 255

Mavromoustakos T., Calogeropoulou T., **Koufaki M.**, Kolocouris A., Demetzos K., Meng Z., Makriyannis A., Balzarini J. De Clercq E.. Ether phospholipid-AZT conjugates possessing anti-HIV and anti-tumor cell activity. Synthesis, conformational analysis and study of their thermal effects on membrane bilayers. *J. Med. Chem.* **2001**, 44, 1702-1709

Koufaki M., Calogeropoulou T., Detsi A., Roditis A., Kourounakis A., Papazafiri P., Tsiakitzis K., Gaitanaki C., Beis I., Kourounakis P. Novel potent inhibitors of lipid peroxidation with protective effects against reperfusion arrhythmias. *J. Med. Chem.* **2001**, 44, 4300-4303

Detsi A., **Koufaki M.**, Calogeropoulou T. Synthesis of (*Z*)-4-hydroxytamoxifen and (*Z*)-2-(4-[1-(p-hydroxyphenyl)-2-phenyl]-1-butenyl)phenoxyacetic acid. *J. Org. Chem.* **2002**, 67, 4608-4611

Avlonitis N., Lekka E., Detsi A., **Koufaki M.**, Calogeropoulou T., Skoulica E., Siapi E., Kyrikou I., Mavromoustakos T., Tsotinis A., Golic Grdadolnik S., Makriyannis A. Antileishmanial Ring-Substituted Ether Phospholipids. *J. Med. Chem.* **2003**, 46, 755-767

Koufaki M., Calogeropoulou T., Rekka E., Chryselis M., Papazafiri P., Gaitanaki C., Makriyannis A. Bifunctional Agents for Reperfusion Arrhythmias. Novel Hybrid Vitamin E/Class I Antiarrhythmics. *Bioorg. Med. Chem.* **2003** *11*, 5209-5219

Koufaki M., Detsi A., Theodorou E., Kiziridi C., Calogeropoulou T., Vassilopoulos A., Kourounakis A., Rekka E., Kourounakis P., Gaitanaki C., Papazafiri P. Synthesis of Chroman Analogues of Lipoic Acid and Evaluation of their Activity against Reperfusion Arrhythmias. *Bioorg. Med. Chem.* **2004**, *12*, 4835-4841

Papazafiri P., Avlonitis N., Angelou A., Calogeropoulou T., **Koufaki M.**, Scoulica E., Fragiadaki I. Structure-activity relationships of antineoplastic ring-substituted ether phospholipid derivatives. *Cancer Chemother. Pharmacol.* **2005**, DOI: 10.1007/s00280-004-0935-6

PATENTS

GR 1003725 "Bifunctional agents possessing antioxidant and antiarrhythmic activity"
Applicants and Inventors: **Maria Koufaki**, Theodora Calogeropoulou, Alexandros Makriyannis

WO 0204438 and EP1301504, CA2415523, US2004259763
"Bifunctional agents possessing antioxidant and antiarrhythmic activity"
Applicant: UNI-PHARMA S.A.
Inventors: **Maria Koufaki**, Theodora Calogeropoulou, Alexandros Makriyannis

US03/34225, WO2004041167 "Antiprotozoal ring-substituted phospholipids" Applicants and Inventors: Theodora Calogeropoulou, **Maria Koufaki**, Nikolaos Avlonitis, Alexandros Makriyannis

GR 20050100100 2/3/2005 "Contrast agents containing anticancer ether phospholipids for the detection of neoplasias by ultrasound" Applicants and Inventors: Theodora Calogeropoulou, **Maria Koufaki**

REVIEWS

Buchholzer F.J., **Koufaki M.**, Tronchet J.M.J. La spectrometrie de masse: Une excellente methode quantitative tres utile en pharmacologie. *Epitheor. Klin. Pharmacol. Farmakokinet. Int. Ed.* **1987**, *1*, 119

Koufaki M., Plessas H., Plessas S. Human insulin: Chemistry, Biosynthesis, Production *Epitheor. Klin. Pharmacol. Farmakokinet. Greek. Ed.* **1989**, *7*, 156

Koufaki M., Buchholzer F.J. Les liposomes comme transporteurs de medicaments. *Epitheor. Klin. Pharmacol. Farmakokinet. Int. Ed.* **1990**, *4*, 12

Calogeropoulou T., Detsi A., Lekkas E, **Koufaki M.** Strategies in the design of prodrugs of anti HIV agents in "Therapeutic strategies against HIV infection" Guest Editor M. Koufaki. *Current Topics in Medicinal Chemistry*, **2003**, *3* (13), 1467

PRESENTATIONS 2000-2005

8^o Panhellenic Symposium of Pharmaceutical Chemistry, Athens, January 2000
Calogeropoulou T., **Koufaki M.**, Detsi A., Hendriks H.R., Makriyannis, A., Syriani, D., Alexis, M.N. Synthesis and biological evaluation of phosphotriester analogs of 4-hydroxytamoxifen.

3rd International Symposium on Angiotensin II Antagonism, London, UK, February 2000 Theodoropoulou E., Marsh D., **Koufaki M.**, Matsoukas J.
Effect of losartan on phosphatidylcholine membranes: comparison with a less biologically active molecule.

3rd World Meeting on Pharmaceuticals, Biopharmaceutics and Pharmaceutical Technology, Berlin Germany, April 2000
Koufaki M., Calogeropoulou T., Detsi A., Kourounakis P., Rekka E., Chrysselis M., Papazafiri P., Tseti J., Makriyannis A. Agents combining antioxidant and antiarrhythmic activity.

A meeting of The Society for Free Radical Research (Europe). Liverpool, UK, July 2000.

Koufaki M., Calogeropoulou T., Detsi, A.; Roditis A., Kourounakis A., Tsiakitzis K., Kourounakis P., Doulias P-T., Galaris D. Synthesis and biological evaluation of novel antioxidants.

XVIth International Symposium on Medicinal Chemistry, Bologna, Italy, September 2000

Koufaki M., Calogeropoulou T., Detsi A., Roditis A., Kourounakis A., Tsiakitzis, K., Kourounakis, P. Novel highly potent antioxidants.

XVIth International Symposium on Medicinal Chemistry, Bologna, Italy, September 2000

Calogeropoulou T., **Koufaki M.**, Detsi A., Fichtner I., Eisenbrand G., Syriani D., Alexis M.N., Hendriks H.R., Makriyannis, A. Phosphorylated analogs of 4-hydroxytamoxifen.

9th Cyprus Conference on New Methods in Drug Research. Limassol, Cyprus, May 2001 Mavromoustakos T., Calogeropoulou T., **Koufaki M.**, Kolokouris A., Daliani I., Demetzos C., Meng Z., Makriyannis A., Balzarini J., De Clerq E. Ether phospholipid-AZT conjugates possessing anti-HIV and anti-tumor cell activity. Synthesis, conformational analysis and study of their thermal effects on membrane bilayers.

7th Conference in advanced Medicinal Chemistry. Thessaloniki, May 2001

Roditis A., Detsi A., Calogeropoulou T., **Koufaki M.**, Kourounakis A., Papazafiri P., Tsiakitzis K., Gaitanaki C., Beis I., Kourounakis P. Novel potent inhibitors of lipid peroxidation with protective effects against reperfusion arrhythmias.

12th European Symposium on Organic Chemistry. Groningen, The Netherlands, July 2001

Detsi A., **Koufaki M.**, Calogeropoulou T. A convenient stereoselective route to (Z)-4-hydroxy tamoxifen.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Athens, January 2002

Detsi A., Roditis A., Calogeropoulou T., **Koufaki M.**, Papazafiri P., Kourounakis A., Tsiakitzis K., Kourounakis P. Design and synthesis of novel compounds for the suppression of reperfusion arrhythmias.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Athens, January 2002

Avlonitis N., Lekka E., **Koufaki M.**, Calogeropoulou T., Scoulaka E., Papazafiri P., Siapi E., Kyrikou I., Mavromoustakos T., Tsotinis A. Design and synthesis of ether phospholipids possessing anticancer and antileishmanial activity

XVIIth International Symposium on Medicinal Chemistry, Barcelona, Spain, September 2002

Koufaki M., Calogeropoulou T., Detsi A., Roditis A., Kourounakis A., Papazafiri P., Tsiakitzis K., Gaitanaki C., Beis I., Kourounakis P. Design and synthesis of novel antioxidants with protective effects against reperfusion arrhythmias.

XVIIth International Symposium on Medicinal Chemistry, Barcelona, Spain, September 2002 Calogeropoulou T., **Koufaki M.**, Avlonitis N., Lekka E., Detsi A., Skoulaka E., Papazafiri P., Siapi E., Kyrikou I., Mavromoustakos T., Tsotinis A., Makriyannis A. Design and synthesis of novel ether phospholipids embodying cyclic moieties. Comparative study of their anticancer and antileishmanial activity.

COST CHEMISTRY D13 WORKSHOP, Lisbon, Portugal October 2003

Avlonitis N., Angelou P., **Koufaki M.**, Calogeropoulou T., Scoulaka E. Antileishmanial Ring-Substituted Ether Phospholipids.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Patras, January 2004

Kiziridi C., **Koufaki M.**, Papazafiri P., Vassilopoulos A. Design and synthesis of novel 5-alkylpiperazinyl benzopyran analogues with potential antiarrhythmic activity.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Patras, January 2004

Angelou P., Avlonitis N., **Koufaki M.**, Fragiadaki I., Scoulaka E., Calogeropoulou T. Design and synthesis of cycloalkylidene-substituted ether phospholipids possessing antiparasitic activity.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Patras, January 2004

Theodorou E., **Koufaki M.**, Nousis L., Galaris D. Synthesis of caffeic acid analogues and 3,4-dihydroxyphenyl analogues with cytoprotective activity.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Patras, January 2004

Melagraki G., Afantitis A., Detsi A., Athanaselis G., Iglessi-Markopoulou O., Kontogiorgis C., Hatjipavlou-Litina D., **Koufaki M.** Design and synthesis of novel coumarin derivatives and evaluation of their antioxidant and antiinflammatory activity.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Patras, January 2004

Bouloubasi D., Detsi A., Zikou L., Athanaselis G., Iglessi-Markopoulou O., Kontogiorgis C., **Koufaki M.**, Hatjipavlou-Litina D. Design and synthesis of novel quinoline derivatives possessing antioxidant and antiinflammatory activity.

10^o Panhellenic Symposium of Pharmaceutical Chemistry, Patras, January 2004

Kapou A., Benetis N., Avlonitis N., Lekka E., Calogeropoulou T., **Koufaki M.**, Nikolaropoulos S., Mavromoustakos T. QSAR of cycloalkyl substituted ether phospholipids.

International Symposium on Advances in Synthetic, Combinatorial and Medicinal Chemistry, Moscow, Russia, May 2004

Koufaki M., Theodorou E., Kiziridi C., Calogeropoulou T., Detsi A., Galaris D., Nouis L., Papazafiri P., Vassilopoulos A. Chroman analogues protecting cells from ischemia/reperfusion or DNA damage.

International Symposium on Advances in Synthetic, Combinatorial and Medicinal Chemistry, Moscow Russia, May 2004

Calogeropoulou T., Koini E., **Koufaki M.**, Vassilopoulos A., Papazafiri P. Design and synthesis of novel 1,4-benzoxazine and 4-aminobenzopyran analogues active against reperfusion arrhythmias.

10th Cyprus Conference on New Methods in Drug Research, Limassol, Cyprus, May 2004

Angelou P., Avlonitis N., Calogeropoulou T., **Koufaki M.**, Scoulica E., Fragiadaki I. Design and synthesis of antileishmanial ring-substituted ether phospholipid derivatives.

1st Panhellenic Symposium on Organic Chemistry, Athens, November 2004

Theodorou E., **Koufaki M.**, Katsanou E., Alexis M.N. Synthesis of catechol analogues with neuroprotective activity.

1st Panhellenic Symposium on Organic Chemistry, Athens, November 2004

Kiziridi C., **Koufaki M.**, Papazafiri P. Synthesis of novel benzopyran analogues bearing class III antiarrhythmic pharmacophores.