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Education

1975-1979: Bachelor of Sciences (**B.Sc.**), Chemistry, (Honors).
Philadelphia College of Textiles and Science. Philadelphia, PA. U.S.A

1979-1984: Doctor of Philosophy (**Ph.D**), Organic Chemistry
University of Pennsylvania. Philadelphia, PA. U.S.A
"Ionophore antibiotic X14547A- Enantioselective synthesis of the tetrahydropyran unit; Studies directed towards the total synthesis of Amphotericin B; Syntheses of O-Glycosides and Glycosyl Fluorides."
Supervisor of Dissertation: Professor K. C. Nicolaou

Fields of Specialization

- Stereocontrolled total synthesis of architecturally complex natural products having significant bioregulatory properties.
- Carbohydrate chemistry.
- Drug design and synthesis.
- New synthetic technology.

Current Research Interests

- Chiroselective synthesis of novel endogenous and natural cannabinoid analogs.
- Development of novel arachidonic acid cascade modulators.
- Development of tissue-specific antiestrogens.
- Fluorine chemistry.
- New synthetic technology enabling the synthesis of conformationally constrained bioactive molecules.
- Organocatalysis: Asymmetric Aldol and Michael reactions in aqueous media.

Appointments

1978-1979: Teaching Assistant – Organic Chemistry, Department of Chemistry, Philadelphia College of Textiles and Science.

1979-1983: Teaching Assistant–Organic Chemistry, Department of Chemistry, University of Pennsylvania.

1983-1984: Research Assistant – Organic Chemistry, Department of chemistry, University of Pennsylvania.

1986-1991: Researcher - Department of Research and Development, Vioryl S.A.

1991-1998: Research Associate, National Hellenic Research Foundation.

1998-2002: Special Functional Scientist, National Hellenic Research Foundation.

2002-2007: Senior Researcher, National Hellenic Research Foundation.

2007- Present: Research Director, National Hellenic Research Foundation.

Teaching Experience

1978-1979: Teaching Assistant – Organic Chemistry, Department of Chemistry, Philadelphia College of Textiles and Science

1979-1983: Teaching Assistant – Organic Chemistry, Department of Chemistry, University of Pennsylvania

1998: Instructor in training seminar on “Modern Chemistry and its Applications” chemistry teachers in secondary education in Greece.

1993-2013: Supervisor of 2 diploma students, 2 post-graduates, 4 M.Sc., 6 Ph.D., and 5 post doctoral fellows (IBMCB).

Other Activities

1993-present: Member of the Greek Chemical Society

1996-present: Member of the Greek Chemical Society, Pharmaceutical Chemistry Division

2001-present: Member of the Organizing Committee of 5 International and 3 Greek Symposia

2005-present: Reviewer in peer-reviewed international journals: Letters in Organic Chemistry, Polymer Chemistry, Letters in Drug Design and Discovery, Journal of Organic Chemistry, Journal of Medicinal Chemistry.

Awards

“Academic Achievement in Science Award”(1977-1978).

“Who is who in American Colleges and Universities Award” (1978-1979).

“Outstanding Foreign Student Award”(1979).

“ American Institute of Chemists Award”, Pennsylvania Section (1979).

Publications

1. "Total Synthesis of Ionophore Antibiotic X-14547A. 1. Enantioselective Synthesis of the Tetrahydropyran and Tetrahydroindan Building Blocks", K.C. Nicolaou, D.P. Papahatjis, D.A. Claremon And R.E. Dolle, III, J. Am. Chem. Soc., 103, 6967-6969 (1981).
2. "Total Synthesis of Ionophore Antibiotix X-14547A. 2. Coupling of the Tetrahydropyran and Tetrahydroindan Systems and Construction of the Butadienyl and Ketopyrrole Moieties", K.C. Nicolaou, D.A. Claremon, D.P. Papahatjis and R.L. Magolda, J. Am. Chem. Soc., 103, 6969-6971 (1981).
3. "A Mild Method for the Synthesis of 2-Ketopyrroles from Carboxylic Acids", K.C. Nicolaou, D.A. Claremon and D.P. Papahatjis, Tetrahedron Letters, 22 (46) 4647-4650 (1981).
4. "A New, Mild and general Method for the Synthesis of O-glycosides", K.C. Nicolaou, S.P. Seitz, D.P. Papahatjis, J. Am. Chem. Soc., 105, 2430 (1983).
5. "Practical Synthesis of Oligasaccharides, Partial Synthesis of Avermectin B1a", K.C. Nicolaou, R.E. Dolle, D.P. Papahatjis and J.L. Randall, J. Am. Chem. Soc., 106, 4189 (1984).
6. "Total Synthesis of Ionophore Antibiotix X-14547A", K.C. Nicolaou, D.P. Papahatjis, D.A. Claremon, R.L. Magolda and R.E. Dolle, J. Org. Chem., 50, 1440 (1985).
7. "Modern Synthetic Technology and Total Synthesis of Bioactive Molecules", K.C. Nicolaou, N.A. Petasis, R.E. Dolle, S.W. Li, D.P. Papahatjis, J. Uenishi, R.E. Zipkin, in "New Methods in Drug Research", A. Makriyannis, Ed., J.R. Prous Science, Barcelona, Ch. 11, pp. 179-200, (1985)
8. "Ionophore Antibiotic X-14547A. Enantioselective Synthesis of the Tetrahydropyran Unit. Studies towards the Synthesis of Amphotericin B. Synthesis of O-Glycosides and Glycosyl fluorides", D.P. Papahatjis, Ph.D. Thesis, University of Pennsylvania (Supervisor: Prof. K.C. Nicolaou), 1984.
9. "Stereocontrolled Construction of Key Building Blocks for the Total Synthesis of Amphoteronolide B and Amphotericin B", K.C. Nikolaou, R.A. Daines, J. Uenishi, W.S. Li, D.P. Papahatjis and T.K. Chakraborty, J. Am. Chem. Soc., 109, 2205 (1987).
10. "Total Synthesis of Amphoteronolide B and Amphotericin B". 1. Strategy and Stereocontrolled Construction of Key Building Blocks, K.C. Nicolaou, R.A. Daines, J. Uenishi, W.S. Li, D.P. Papahatjis, and T.K. Chakraborty, J. Am. Chem. Soc., 110, 4672 (1988).
11. "Enhanced Optical Purity of 3-Hydroxy-esters Obtained by Baker's Yeast Reduction of 3-Ketoesters", V. Spiliotis, D.P. Papahatjis and N. Ragoussis, Tetrahedron Letters, 31, (11) 1615-1616 (1990).

12. "A brief review of the recent achievements in the field of Cannabinoids with main emphasis on the synthesis of lead compounds and their interactions on lipid bilayers", T. Mavromoustakos, D.P. Papahatjis, T. Kourouli, E. Theodoropoulou, A. Makriyannis, Rev. Clinical Pharmacology, 13, 105 (1995).
13. "Study of Thermotropic properties of Cannabinoids in Phosphatidylcholine bilayers using Differential scanning Calorimetry and Small Angle X-ray Diffraction", T. Mavromoustakos, D.P. Papahatjis, E. Theodoropoulou, T. Kourouli, De-Ping Yang, M. Trumbore, A. Makriyannis, Biochim. Biophys. Acta, 1281, (2) 235-244 (1996).
14. "Pharmacophoric Requirements for Cannabinoid Side chains. Naphthoyl and Naphthylmethyl substituted Δ^8 -THC Analogs.", D.P. Papahatjis, T. Kourouli and A. Makriyannis, J. Heter. Chem. 33, 559- 562 (1996).
15. "Pharmacophoric Requirements for Cannabinoid Side Chains. Multiple bond and C1' -Substituted Δ^8 -Tetrahydrocannabinols", D.P. Papahatjis, T. Kourouli, V. Abadji, A. Goutopoulos and A. Makriyannis, J. Med. Chem. 41, 1195 (1998).
16. "Novel Analogues of Arachidonylethanolamide (Anandamide): Affinities for the CB1 and CB2 Cannabinoid Receptors and Metabolic Stability." S. Lin, A. T. Khanolkar, P. Fan, A. Goutopoulos, Ce Qin, D.P. Papahatjis, and A. Makriyannis, J. Med. Chem. 41, 5353 (1998).
17. "Structure Elucidation and Conformational Properties of Synthetic Cannabinoids 2-[6a,7,10,10a-tetrahydro-6,6,9-trimethyl-6H dibenzo[b,d]pyran-1-ol]-2-[hexyl]-1,3-dithiolane and its methylated analog" T. Mavromoustakos, E. Theodoropoulou, M. Zervou, T. Kourouli and D.P. Papahatjis. J. Pharm. Biomed. Analysis.18, 947 (1999).
18. "A New Ring-Forming Methodology for the Synthesis of Conformationally Constrained Bioactive Molecules" Demetris P. Papahatjis, Spyros Nikas, Andrew Tsotinis, Margarita Vlachou and Alexandros Makriyannis. Chemistry Letters 3, 192 (2001).
19. "Differential membrane fluidization by active and inactive cannabinoid analogs" T. Mavromoustakos, D.P. Papahatjis, P. Laggner. Biochimica et Biophysica Acta 1512, 183 (2001).
20. "Novel 1',1'-Chain Substituted Δ^8 -Tetrahydrocannabinols" Demetris P. Papahatjis, Spyros P. Nikas, Thanos Andreou and Alexandros Makriyannis. Biorganic and Medicinal Chemistry Letters. 3583, (2002).
21. "Pharmacophoric Requirements for Cannabinoid Side Chains. 3: Probing the Cannabinoid Receptor subsite at C1'" Demetris P. Papahatjis, Spyros P. Nikas, Therapia Kourouli, Ravi Chari, Wei Xu, Roger G. Pertwee and Alexandros Makriyannis. J. Med. Chem. 46, 3221, (2003).
22. "The Role of Halogen Substitution in Classical Cannabinoids. A CB1 Pharmacophore Model." Spyros P. Nikas, Jolanta Grzybovska, Demetris P. Papahatjis, Avgui Charalambous, Ali R. Banijamali, Ravi Chari, Pusheng Fan,

- Therapia Kourouli, Sonyuan Lin, Albert J. Nitowski, Gilbert Marciniak, Yan Guo, Xiuyan Li, Chia-Lin J. Wang and Alexandros Makriyannis. AAPS, Journal. 6(4): Article 30 (2004).
23. "Preclinical behavioral evaluation of a novel cannabinoid analogue" Antoniou K, Galanopoulos A, Vlachou S, Nahmias V, Thermos, K, Panagis G, Daifoti Z, Marselos M, Papahatjis D, and Spyraiki C. Rev. Clinical Pharmacology and Pharmacokinetics, 23, 26 (2005).
 24. "Behavioral pharmacological properties of a novel cannabinoid 1',1'-dithiolane Δ^8 -THC analogue, AMG-3." Antoniou K, Galanopoulos A, Vlachou S, Kourouli T, Nahmias V, Thermos, K, Panagis G, Daifoti Z, Marselos M, Papahatjis D, and Spyraiki C. Behavioral Pharmacology. 16, 499 (2005).
 25. "A Convenient Preparation of Enantiomerically Pure Esters of trans-Epoxy succinic Acid" D.P. Papahatjis, T. Kourouli, Victoria Nahmias. Letters in Organic Chemistry, 3, 45 (2006).
 26. "Structural Modifications of the Cannabinoid Side Chain towards C3-Aryl and 1',1'-Cycloalkyl-1'-Cyano Cannabinoids" Demetris P. Papahatjis, Victoria R. Nahmias, Thanos Andreou, Pusheng Fan, and Alexandros Makriyannis. Biorganic and Medicinal Chemistry Letters. 1616, (2006).
 27. Patent application No 20050100282/08-06-2005/O.B.I.: "Tissue specific antiestrogens selective for estrogen receptor alpha" - Alexis MN, Papahatjis D, Assimomitis N, Siriani D, Sekeris CE.
 28. "Mapping the Melatonin Receptor. 7. 8-Substituted *N*-Acyl-5-methoxytryptamines and 8-substituted *N*-Acyl-5-methoxy-1-methyltryptamines: N-butanoyl 5-methoxy-1-methyl-8,8-trimethylenetryptamine (12c), a human MT₂ agonist that is an antagonist at the human MT₁ receptor. Andrew Tsotinis, Margarita Vlachou, Demetris P. Papahatjis, Theodora Calogeropoulou, Spyros Nikas, Peter J. Garratt, Vincent Piccio, Stefan Vonhoff Kathryn Davidson, Muy-Teck Teh and David Sugden. J. Med. Chem. 49, 3509, (2006).
 29. "Pharmacological characterization of novel ligands for CB1 and CB2 cannabinoid receptors" Thermos K, Papazoglou M, Antoniou K, Mastrodimou N, Panagis G, Vlachou S, Renieri E, Nahmias V, Menissiou A, Gianni M, Kondylis MP, Daifoti-Papadopoulou Z, Papahatjis D, Spyraiki C Acta Pharmacologica Sinica, 27: 394-395 Suppl. 1, Jul (2006).
 30. "An Efficient Synthesis of Simple β,β' -Cyclobisalkylated Melatonergic Phenylalkylamides" Andrew Tsotinis, Margarita Vlachou, Demetris P. Papahatjis, Spyros P. Nikas and David Sugden. Letters in Organic Chemistry, 4, 92 (2007).
 31. "The C1'-Cycloalkyl Side Chain Pharmacophore in Tetrahydrocannabinols". Demetris P. Papahatjis, Victoria R. Nahmias, Spyros P. Nikas, Thanos Andreou,

- Shakiru O. Alapafuja, Andrew Tsotinis, Jianxin Guo, Pusheng Fan, and Alexandros Makriyannis. J. Med. Chem. 50, 4048, (2007).
32. "The Applications of 3D-QSAR Studies for Novel Cannabinoid Ligands Substituted at the C1' Position of the Alkyl Side Chain on the Structural Requirements for Binding to CB1 and CB2 Receptors" Serdar Durdagi, Agnes Kapou, Therapia Kourouli, Thanos Andreou, Spyros P. Nikas, Victoria R. Nahmias, Demetris P. Papahatjis, Manthos. G. Papadopoulos and Thomas Mavromoustakos. J. Med. Chem. 50, 2875, (2007).
 33. "Cannabilactones: A Novel Class of CB2 Selective Agonists with Peripheral Analgesic Activity" Atmaram D. Khanolkar, Dai Lu, T. Philip Malan, Jr., Mohab Ibrahim, Frank Porreca, Ganesh A. Thakur, Vijayabaskar Veerappan, Richard I. Duclos, Jr., Xiaoyu Tian, Clifford George, Damon A. Parrish, Demetris Papahatjis and Alexandros Makriyannis. J. Med. Chem. 50, 6493, (2007).
 34. "Combined 3D QSAR and molecular docking studies to reveal novel cannabinoid ligands with optimum binding activity" Durdagi, S., Papadopoulos, M.G., Papahatjis, D.P., Mavromoustakos, T. Biorganic and Medicinal Chemistry Letters. 6754, (2007).
 35. "Novel ligands for cannabinoid receptors: Pharmacological studies" Antoniou K, Chouliara, O, Polissidis, A, Papalexi, E. Papazoglou M, Mastrodimou N, Panaqis G, Vlachou S, Renieri E, Nahmias V, Menissiou A, Gianni M, Kondylis MP, Thermos K., Daifoti-Papadopoulou Z, Papahatjis D, Spyraiki C Behavioral Pharmacology. 18, supp.1, 24 (2007).
 36. "Testing the 3D QSAR/ComFA-CoMSIA results of flexible bioactive compounds with molecular docking studies" Serdar Durdagi, Catherine Koukoulitsa, Agnes Kapou, Therapia Kourouli, Thanos Andreou, Spyros P. Nikas, Victoria R. Nahmias, Demetris P. Papahatjis, Manthos. G. Papadopoulos and Thomas Mavromoustakos. Drugs of the Future, 32, supp A, 79 (2007).
 37. "Putative Bioactive Conformers of Small Molecules: A Concerted Approach using NMR Spectroscopy and Computational Chemistry" T. Mavromoustakos, S. Golic Grdadolnik, M. Zervou, P. Zoumpoulakis, C. Potamitis, A. Politi, E. Mantzourani, J.A. Platts, C. Koukoulitsa, P. Minakakis, G. Kokotos, T. Tselios, J. Matsoukas, S. Durdagi, M. G. Papadopoulos, D. P. Papahatjis, Z. Spyraiki, G.A. Dalkas, G.A. Spyroulias, In: *Medicinal Chemistry Research Progress*, G.P. Colombo and S. Ricci (Eds.), (2008), Nova Science Publishers, Inc.
 38. "Design and Synthesis of (13S)-Methyl Substituted Arachidonic Acid Analogs: Templates for Novel Endocannabinoids" Demetris P. Papahatjis, Victoria R. Nahmias, Spyros P. Nikas, Marion Schimpfen, Alexandros Makriyannis. CHEMISTRY - A European Journal. 16/13, 4091, (2010).

39. "Novel 1'-1' Chain Substituted Hexahydrocannabinols: 9 β -Hydroxy-3-(1-hexyl-cyclobut-1-yl)-hexahydrocannabinol (AM2389) a Highly Potent Cannabinoid Receptor 1 (CB1) Agonist". Spyros P. Nikas, Shakiru O. Alapafuja, Ioannis Papanastasiou, Carol A. Paronis, Vidyanand G. Shukla, Demetris P. Papahatjis, Anna L. Bowman, Aneetha Halikhedkar, Xiuwen Han, and Alexandros Makriyannis. *J. Med. Chem.* **53**, 6996–7010, (2010).
40. "The cannabinoid CB1 receptor biphasically modulates motor activity and regulates dopamine and glutamate region dependently". Alexia Polissidis, Andreas Galanopoulos, George Naxakis, Demetris Papahatjis, Zeta Papadopoulou-Daifoti, Katerina Antoniou. *The International Journal of Neuropsychopharmacology*. **16** (02), 393-403, (2013).

Presentations

38 PRESENTATIONS IN INTERNATIONAL SYMPOSIA

12 PRESENTATIONS IN NATIONAL SYMPOSIA

Research funding in the last 10 years

- *Excellence in the Research Institutes* (2002-05) "Novel strategies against neurodegeneration" 200000 €. Participant. Important contribution in the preparation of the proposal.
- *GSRT programme Location and use of research results by the creation of new enterprises (Spin-off, 2003-05)* "Cannabinomimetic Analogs with Therapeutic Applications " 44000 €. Coordinator
- *Operational Programme for Competitiveness, GSRT YB/60* (2004-07). "Exploitation of novel cannabinoid analogs with possible analgesic, psychomotor and anti-abuse potential". 106000 €. Coordinator
- *Excellence in the Research Institutes* supervised by the Greek General Secretariat for Research and Technology EPAN 3.3.1. (2006-2009). 1125000 €. Participant
- *EU MARIE CURIE EARLY STAGE TRAINING (EST)* (2006-10) "A European Research Training Site for the Design and Synthesis of Novel Neuroprotective and Hypoglycaemic Agents through a Multi-disciplinary approach." 900000 €. Participant
- *REGPOT-2009-1/ARCADE 245866* (2010-13) 2500000 €. Work Package leader, participation in the committees for the upgrade of the infrastructure of IOPC.
- *Professional Services Agreements with Northeastern University on behalf of its Center for Drug Discovery.* (2008-2010). "a) Multistep synthesis of bicyclic and

tricyclic cannabinoids. b) Synthesis of inhibitors of FAAH and/or MGL. Total budget 73000 €. Coordinator

- *Professional Services Agreements with UNI-PHARMA. S.A. (2011-2012)*. Budget 18200 €. Coordinator