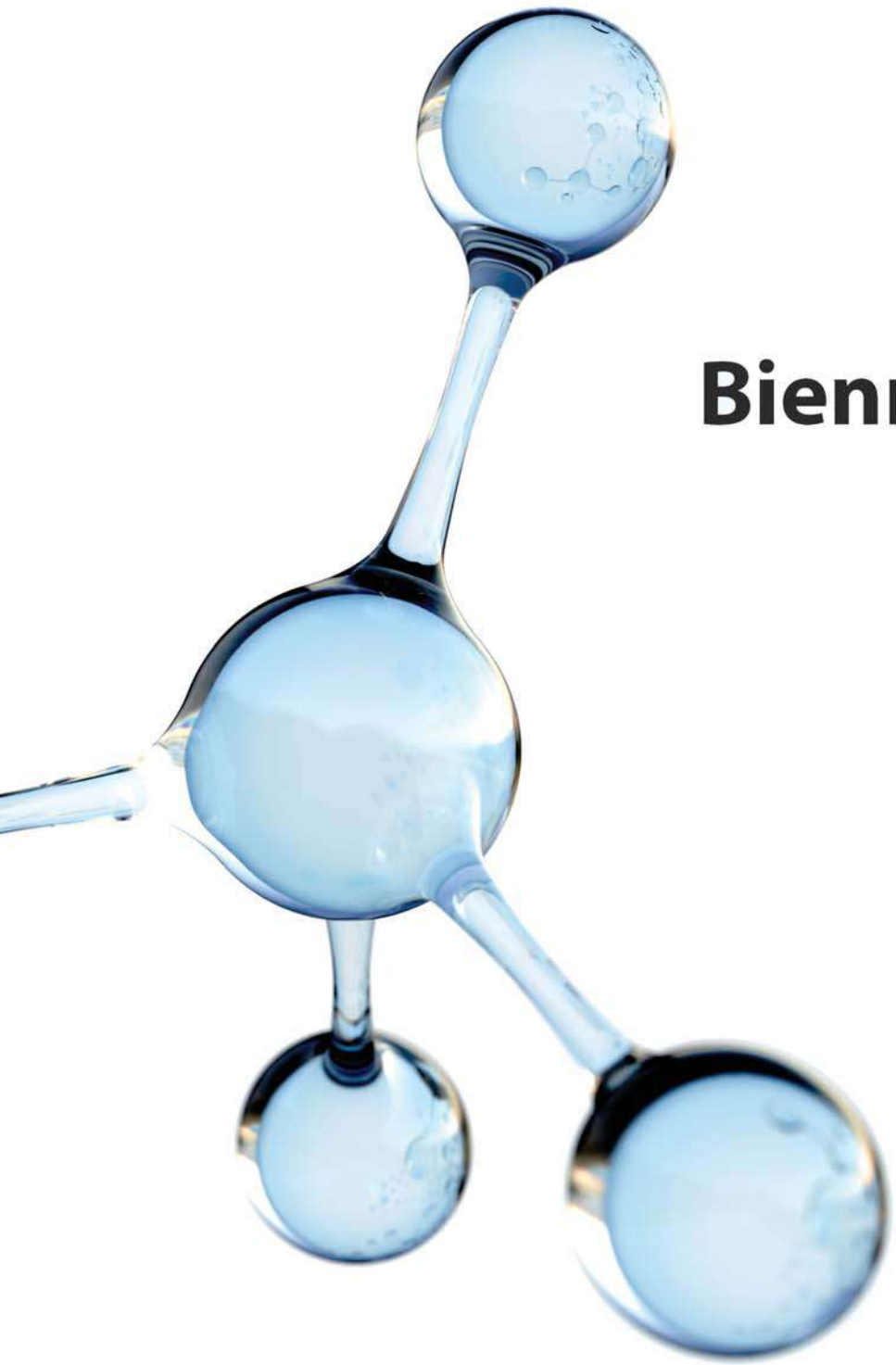
iQAC



Biennial Report
2012 - 2013

CSIC
Consejo Superior de Investigaciones Científicas

Index

Director's Foreword		5
1. Structure and General Results	• History	9
	• Institute Board Members / Administration / "Ad honorem" members	10
	• Departments and Research Groups / IQAC Facilities	11
	• General data: Funding, Scientific Outputs, Outreach activities, Ph. D. Thesis.	12
2. Department of Biological Chemistry and Molecular Modelling	• Nutraceuticals and Free Radicals	26
	• Biotransformation and Bioactive Molecules	30
	• Supramolecular Chemistry	35
	• Ecological Chemistry	39
	• Theoretical and Computational Chemistry	44
	• Bioorganic Chemistry	48
	• Biologically Active Phytochemicals	51
3. Department of Biomedicinal Chemistry	• Research Unit on Bioactive Molecules	56
	• Synthesis and Biomedical Applications of Peptides	61
	• Unit of Glyconjugate Chemistry	65
	• Chemical Biology	67
	• Medicinal Chemistry	70
4. Department of Chemical and Biomolecular Nanotechnology	• Nanobiotechnology for Diagnostics	78
	• Nucleic Acids Chemistry	82
	• Colloid and Interfacial Chemistry	88
	• Cell Therapy	94
	• Surface Chemistry	97
5. Department of Chemical and Surfactants Technology	• Minimization of Industrial Wastes: Isolation of High Added-Value Biopolymers	106
	• Development of Non-Contaminant Industrial Processes	110
	• Statistical Modelling and Fibre Physics	112
	• Biocompatible Surfactants	114
	• Environmental Chemistry of Surfactants and Ionic Liquids	118
	• Physical Chemistry of Surfactant Systems	121
	• Biophysics of Lipids and Interphases	124
6. Collaborative leave at University of Regensburg		137
7. Facilities and Knowledge Transfer	• Custom Antibody Service (CAbS)	140
	• Characterization of Colloidal Dispersion Service	141
	• Microanalysis Service	144
	• Biodegradation and Aquatic Toxicity Service	144
	• Skin Absorption and Skin Efficacy Services	145
	• Synthesis of High Added Value Molecules Service	146
	• Proteomics Service	147
	• Thermal Analysis Service	148
	• SAXS-WAXS Service	148
	• Magnetic Resonance Service	149
	• Lipidomics and UPLC-TOF	150
	• Knowledge Transfer	151
8. Annexes		153

Director's Foreword

The Institute of Advanced Chemistry of Catalonia (IQAC) is one of the research centers of the Consejo Superior de Investigaciones Científicas (CSIC). The Institute is located in Barcelona and it was created to do research of excellence focused on basic chemical sciences, but also addressed to solve specific problems of our society by using tools from the chemistry-biology interface, theoretical chemistry, chemical and biomolecular nanotechnology and sustainable chemistry. In particular, the identification of niches where our expertise can make important contributions is systematically pursued. Equally important to all of us is to be in a permanent attitude to transfer our knowledge and technology results to the industrial sector.

The present Report covers the biennium 2012-2013 giving account of our research activity and of the main results obtained during this period.

These two years have witnessed the first change in the Direction of the Institute from the creation of the institute in 2007. Noticeably, the change in leadership has been accompanied by the economical crisis that affected the amount of funds coming from both the public and industrials sectors to support the research activity all over the country.

These changes did not affect the scientific output of the institute; on the contrary, scientists stepped up with a higher level of dedication to achieve excellent results.

During 2012-2013 the Institute has achieved the highest number of publications (more than 150 per year) as well as the highest average impact factor (4.2) with 5 papers published in Nature group journals and 8 papers published in journals with an impact factor higher than 10.

In addition to the information given here, we invite you to navigate our website (www.iqac.csic.es). There, you will find additional information about the research problems that we face and their results and perspectives. The web page contains also details about the facilities and methodologies that we can offer to the scientific community, both from the public and the private domains, to complement or improve their own projects, or those that can be put in the frame of a joint initiative. In this sense, the research groups and technical services from our Institute will be wide open to attend your inquiries and to offer their best efforts to find adequate responses to your needs, based on their background and expertise.

Ramon Eritja / Àngel Messeguer
Directors of IQAC

Structure and General Results

History

The Institute was created in 2007 to better accommodate the interests of scientists of the Chemistry areas working at the "Center of Investigation and Development" (CID) and to provide a greater external projection of the activities of these scientists within the frame of the Spanish Research Council (CSIC). In spite of its recent creation, the Institute inherits the long and fruitful research tradition in Organic Chemistry initiated by Prof. José Pascual Vila since 1940. After finalizing his activity in the University, in 1967 Prof. Pascual Vila moved with his co-workers of CSIC into the Institute of Organic Chemistry of Barcelona in CID. At the same time, CSIC scientists working on Chemical Technology, such as those related to the textile and leather fields, were also incorporated into CID. During many years the CID has been the referent of the CSIC Chemistry in Catalonia and of the organic and bioorganic chemistry research in our community. Many graduate students and postdocs formed in this Center have moved to relevant positions in academic institutions (Universities, CSIC) and in private sector. In 1996, a joined action of the bioorganic, theoretical and technological groups together with those working in chemical issues related to the environment, led to the creation of the Institute of Chemical and Environmental Research "Josep Pascual Vila" (IIQAB). During the ten-year period of IIQAB, research groups have adapted their objectives to the new demands of society and new groups have also been generated. From these efforts, the Biological Chemistry, Theoretical and Computational Chemistry, Sustainable Chemistry and selected items of Chemical Technology have been reinforced. Concomitantly, potent groups working on Chemical and Biomolecular Nanotechnology have emerged or have been incorporated into IQAC. Actually, this set of scientific interests, in which the apparent heterogeneity of the active research areas is clearly compensated by the wide opportunities of their mutual interaction, justifies the creation of IQAC as a solid and modern Institute that looks at the future leaning on two pillars: the enthusiasm and expertise of its personnel and the robustness of the Chemistry tradition in our Centre.

Although its creation was in 2007, the research groups incorporated into IQAC have a recognized international prestige in their research fields. Among others, it should be highlighted the design, synthesis and evaluation of molecules of therapeutic, pharmacological or biological interest, the chemistry and applications of surfactants, the study of hormones and enzymatic transformations in insects, the development of environmentally friendly technologies, the treatment of industrial waste, the research in peptides and proteins, the theoretical study in electronic structure, or the application of nanotechnological approaches to the understanding of nanoscale systems and the development of novel nanomaterials and nanodevices, such as bioanalytical tools based on the combination of tailored bioreceptors, new nucleic acid derivatives and well-defined nanostructures and advanced materials.

In addition, our Institute has a set of scientific and technical facilities that offer services to the IQAC research groups as well as to groups or companies from elsewhere: Thermal Analysis and Calorimetry, Magnetic Resonance (NMR and EPR), Organic Microanalysis, Synthesis of High-Added Value Molecules, X-Ray Dispersion at Small Angle (SAXS-WAXS), Characterization of Colloidal Dispersions, Percutaneous Absorption and Skin Efficacy, Monoclonal Antibodies Production and Characterization (CAbS), Biodegradation and Aquatic Toxicity, Lipidomics and UPLC-TOF, Proteomics and Technology transfer.

Institute Board Members

Àngel Messeguer Peypoch
Director 2012

Ramon Eritja Casadellà
Director 2013

Rosa Infante Martínez-Pardo
Deputy Director 2012

Ramon Pons Pons
Deputy Director 2013

Joan Ricard Ibáñez Villar
Head of Administration

Jesús Joglar Tamargo
Head of Department of Biological Chemistry and Molecular Modelling

Gemma Fabriás Domingo / Amadeu Llebaria Soldevila
Heads of Department of Biomedicinal Chemistry

Jordi Esquena Moret
Head of Department of Chemical and Biomolecular Nanotechnology

Ramon Pons Pons / Maria Teresa García Ramon
Heads of Department of Chemical and Surfactants Technology

Jaume Caelles Balcells
Personnel Representative

Avencia Diez Ortego
Personnel Representative

Meritxell Martí Gelabert
Personnel Representative

Josep Carilla Auguet / Pilar Domènech Duran
Invited Services Representative

Administration

Director:
Angel Messeguer Peypoch/ Ramon Eritja Casadellà

Deputy Director:
Rosa Infante Martínez-Pardo/ Ramon Pons Pons

Head of Administration:
Joan Ricard Ibáñez Villar

Secretaries:
Lídia Beltran Fabregat
Leonor Moliner Ferrer

«Ad honorem» members

Jaume Cot Cosp

Departments and Research Groups

Department of Biological Chemistry and Molecular Modelling

- Nutraceuticals and Free Radicals
- Biotransformation and Bioactive Molecules
- Supramolecular Chemistry
- Chemical Ecology Unit (CEU)
- Theoretical and Computational Chemistry
- Biologically Active Phytochemicals
- Applied Biocatalysis and Biodegradation
- Bioorganic Chemistry

Department of Biomedicinal Chemistry

- Research Unit on BioActive Molecules
- Synthesis and Biomedical Applications of Peptides
- Unit of Glycoconjugate Chemistry
- Medicinal Chemistry
- Chemical Biology

Department of Chemical and Biomolecular Nanotechnology

- Nanobiotechnology for Diagnostics
- Nucleic Acids Chemistry
- Colloid and Interfacial Chemistry
- Surface Chemistry
- Cellular Therapy

Department of Chemical and Surfactants Technology

- Minimization of Industrial Wastes: Isolation of High Added-Value Biopolymers
- Development of Non-contaminant industrial processes
- Statistical Modelling and Fibre Physics
- Biocompatible Surfactants
- Environmental Chemistry of Surfactants and Ionic Liquids
- Physical Chemistry of Surfactant Systems
- Biophysics of Lipids and Interphases
- Textile and Cosmetic Innovations
- Plasma Chemistry

Collaborative Leave at University of Regensburg

- David Diaz Diaz

IQAC Facilities and Technology Transfer

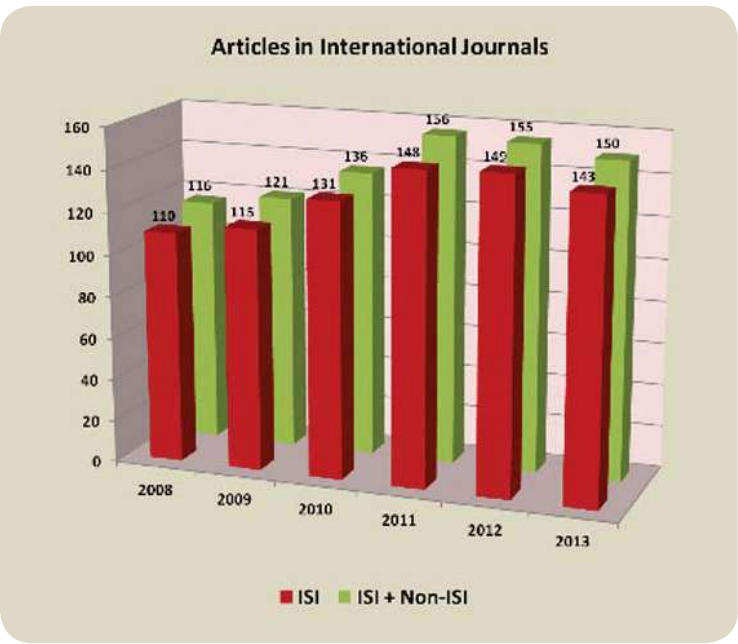
- Custom Antibody Service (CAbS)
- Characterization of Colloidal Dispersion Service
- Microanalysis Service
- Biodegradation and Aquatic Toxicity Service
- Skin Absorption and Skin Efficacy Services
- Synthesis of High Added Value Molecules Service
- Proteomics Service
- Thermal Analysis Aervice
- SAXS-WAXS Service
- Magnetic Resonance Service
- Lipidomics and UPLC-TOF
- Knowledge Transfer

PERSONNEL	Staff	Technicians	Postdocs	Ph. D. Students + undergrads
BCMM	16	3	9	29
BMC	9	4	2	24
CBN	9	4	19	41
CST	14	13	6	18
Services	3	5		
TOTAL	51	28	36	112

SCIENTIFIC OUTPUT	ISI Journals	Non-ISI int	Non-ISI nat	Book ch.
BCMM	97	2		6
BMC	49	2		1
CBN	119	5	1	10
CST	66	2	0	
TOTAL	**331**	11	1	17

ACADEMIC OUTPUT	PhD Thesis	Courses	Conferences
BCMM	10	2	6
BMC	3	1	3
CBN	13	7	5
CST	2	9	3
TOTAL	28	19	17

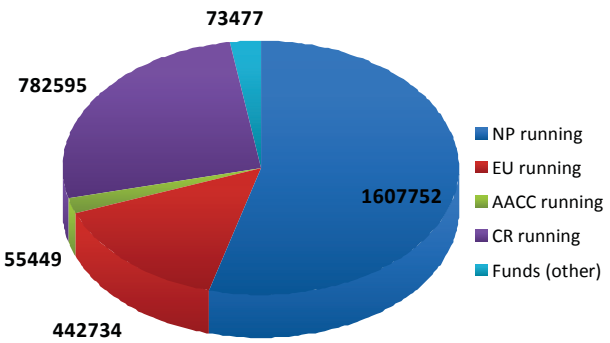
Evolution of the number of articles in the past six years



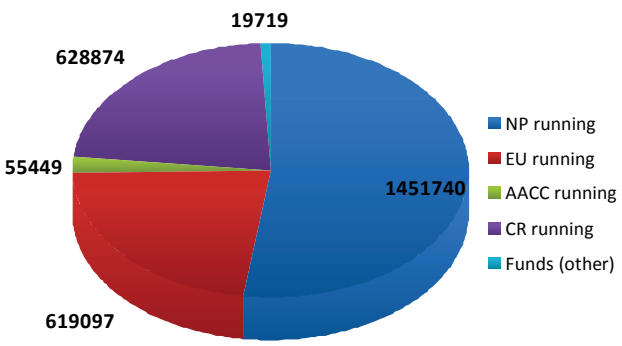
Competitive funds

PROJECTS	2012	budget	2013	budget
NP running	44	1607752	41	1451740
EU running	16	442734	8	619097
AACC running	5	55449	5	55449
CR running	36	782595	28	628874
Funds (other)	3	73477	3	19719
TOTAL		**2962007**		**2774878**
NP: National Project; EU: European Union; AACC: Autonomous Community; CR: Contracted Research				

Budget in 2012

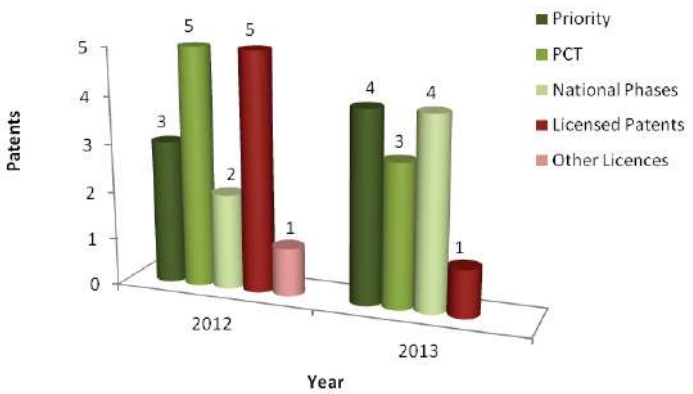


Budget in 2013



TECHNOLOGICAL OUTPUT	2012	2013	Total
Priority	3	4	7
PCT	5	3	8
National Phases	2	4	6
Licensed Patents	5	1	6
Other licences	1	-	1
TOTAL	16	12	28

Patents 2012-2013



Partnerships and institutional agreements

Four groups of IQAC belongs to the Biomedical Research Networking center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN). This network is one of nine CIBER consortia in Spain, created under the leadership of the Carlos III Health Institute (ISCIII) to promote research excellence and build a critical mass of researchers in the field of Biomedicine and Health Sciences. The research programs of the CIBER-BBN are: Bioengineering and biomedical imaging, Biomaterials and tissue engineering and Nanomedicine, with the Centre's research aimed at developing both systems for prevention, diagnosis and monitoring and related technologies for specific treatments such as Regenerative Medicine and Nanotherapies.

Two groups of IQAC constitute the colloidal and interfacial chemistry unit (QCI) in the TECNIO network. TECNIO is the umbrella brand for Catalan Technology Centres and University Research Groups dedicated to industrial research and technology transfer. TECNIO offers access to cutting edge R&D capabilities: key technologies and knowledge for improving industrial competitive position, providing a wide range of support services for technological innovation, selected under rigorous quality criteria.

2013. Bilateral agreement between l'IQAC-CSIC and the University de Regensburg to support the incorporation of IQAC researcher Dr. David Díaz at the University de Regensburg. Dr. Díaz was appointed as DFG Heisenberg Professor (W2 professor).

2012-2013. Collaborative agreement between IQAC and Canigó Highschool (Col.legi Canigó, Barcelona) to develop motivation and interest for chemistry to highschool students by the performance of practical works at the IQAC laboratories.

2012-2013. Participation of IQAC in the spanish goverment inicitiative to promote ambitious collaborative research between spanish industries and academic institutions known as "CENIT initiative. IQAC participates in two consortia: Dendria and Fenix.

2012. Cooperation Agreement between "Comité Español de Detergencia, Tensioactivos y Afines" (CED), in Barcelona and IQAC in order to enhance collaboration between industry and academic research in the surfactants field.

New instrumentation

2012. Optical Microscopy of lateral high resolution and spectral analysis for the study of nanostructured materials.

2013. Remodelation of the main hall of the building with the mural "Homenage to the chemical elements" of Eugènia Balcells with the presence of the artist, the president , vice-president and institutional delegate of CSIC in Catalonia.

Awards, Certifications, Spin-offs

2012. The Journal Bioanalysis highlights a study from the NQD Group on the detection of steroids.

2012. María José Gómara member of the Organizing committee and Isabel Haro member of the scientific committee. XV International Symposium on Luminescence Spectrometry – Biophysical and Analytical Aspects, 19-22 June 2012, Barcelona.

2012: Licence and development agreement between CSIC and UNISENSOR SA for the Exploitation of the Immunoreagents for Fluoroquinolone Antibiotics.

2012. Lilly Price to the best poster presentation to Joan Atcher (superviser: Ignacio Alonso) at the I Biennial Meeting of the Chemical Biology Group (RSEQ), Santiago de Compostela, Spain on March 8-9, 2012. Title: "Effect of Salt on a Dynamic Combinatorial Library based on Pseudopeptidic Dithiols".

2012 UNE-EN-ISO 9001:2008 certification awarded to Skin absoprtion ans skin efficacy sercices.

2012. Fundation of BICOSOME S.L., an spin-off of CSIC Fundación founded by several researchers of the Dpt of Chemical and Surfactants Technology.

2013. Best poster awards at Select Biosciences Congress, given at Barcelona on the 5-6 March. Carme Pastells and Gloria Colom (supervised by Pilar Marco). Title of the posters: "A Novel Immunochemical Approach for the Diagnosis of Infectious Diseases Caused by Pseudomonas aeruginosa" and "Development of a Multiplexed Fluorescente Microarray for Cardiovascular Biomarker Detection.

2013. Isabel Haro is selected as guest editor of an special issue of the journal "Current Topics in Medicinal Chemistry" (Vol. 13, issue 6, March 2013): "Rheumatoid Arthritis: Current Advances in Pathogenesis, Diagnosis and Therapy".

2013: Exploitation Agreement between CSIC and BIOO Scientific Corporation for the Immunoreagents for Sulfonamide Antibiotics.

2013. National Price in technology Clodomiro Picado Twight", at Costa Rica, awarded to Carlos Rodríguez Rodríguez (superviser: Gloria Caminal).

Journal covers

2012. Journal cover. L. Yi, Y. X. Chen, P. C. Lin, H. Schroder, C. M. Niemeyer, Y. W. Wu, R. S. Goody, G. Triola and H. Waldmann, Chem Commun (Camb) 2012, 48, 10829-10831.

2013. Journal cover. I. Gómez-Pinto, E. Vengut-Climent, R. Lucas, A. Aviñó, R. Eritja, C. González, J.C. Morales. Chem. Eur. J., 19(6), 1920-1927 (2013).

2013. Journal cover. A. Yang, Y. Li, S. Pantoom, G. Triola and Y. W. Wu, Chembiochem 2013, 14, 1296-1300.

2012. Back Cover. Martins-Costa MTC, Anglada JM, Francisco JS, Ruiz-Lopez MF. Angew. Chem. Int. Ed., 124(22), 5600, 2012.

2012. Journal cover. A.L. Barrán-Berdón, M. Muñoz-Úbeda, C. Aicart-Ramos, L. Pérez, M.R. Infante, P. Castro-Hartmann, A. Martín-Molina, E. Aicart, E. Junquera. Soft Matter, 8, 3368-3380, 2012

Organization of scientific meetings

C. Solans, J. Esquena. Organization of the Workshop "Nano-biocolloidal materials and non-equilibrium self-assembly" COST action CM1101, IQAC, Barcelona, Spain, 18-19/06/2012.

J.L. Parra. Organization of the European Epidermal Barrier Research Network 2012. Venecia, Italy. 09/2012.

R. Eritja. Organization of the congress "Conformational diversity and applications of G-quadruplexes. COST Action MP0802, 6-8/10/2012, Sitges (Barcelona). 140 attendees.

C. Solans, J. Esquena. Organization of Jornada QCI (IQAC-CSIC) "Innovar per Resoldre Reptes en la Formulació de Productes", Barcelona, Spain, 26/10/2013.

Participation in committees

2012. Dr. Angel Messeguer es selected to be a member of the Institut de Estudis Catalans as well as delegate at the Calatan Society of Chemistry.

2012. Dr. Angel Messeguer member of the CSIC Council (Consell Rector del CSIC).

2013. Dr. F. Comelles. Member of the Scientific Committee for the 43th workshop of the Spanish Society of detergence.

2013. M. T. García and F. Comelles. Members AENOR CTN 55B Committee. Superficial agents.

2013. Dr. M. T. Garcia. Member of the Jury for the Xavier Domingo's Price. UB-CED. 1ª Edition.

2013. R. Eritja. Organizing Comittee of the 5th European Conference Chemistry for Life Sciences, Barcelona, Spain. 10-12/06/2013.

Invited oral communications

C. Solans. 14th IACIS International Conference on Surface and Colloid Science (Sendai, Japan. 13/5/2012). The key role of surfactant molecular assemblies in nano-emulsion formation by low-energy methods.

J. M. Anglada. 22st International Symposium on Gas Kinetics (GK2012), Boulder Colorado, USA, 17-22/06/2012. The gas phase reactivity of hydroxyl radical in the atmosphere. Hydrogen atom transfer versus proton coupled electron transfer processes.

R. Eritja. International Congress of the Spanish Biophysical Society (SBE Barcelona 2012), Barcelona, 3-6/7/2012 "Origami DNA shows the importance of the correct folding of the quadruplex structure of the thrombin-binding aptamers (TBA) for thrombin interactions."

I. Haro. X Symposium de la Sociedad Española de Química Terapéutica, Highlights in drug discovery from Academia to industry. Segovia, 26/10/2012. The use of citrullinated peptides for the diagnosis and prognosis of rheumatoid arthritis.

J. Coll. Conference. Special IQAC event, IQAC, Barcelona, Spain. 28/02/2013. "Gairabé tota una vida".

I. Ribosa. 43th Jornadas CED. Barcelona, 04/2013. Interaction of Nonionic Surfactants and Hydrophilic Ionic Liquids in Aqueous Solutions.

M. T. Garcia, COST Action TD1203, Dublin, Ireland, 05/2013. Biodegradation Studies of Ionic Liquids.

G. Triola. 5th European Conference Chemistry for Life Sciences, Barcelona, Spain. 10-12/06/2013. Site-Specific, Reversible and Fluorogenic Immobilization of Proteins on Flash-Modified Surfaces.

C. Fàbrega. 5th European Conference Chemistry for Life Sciences, Barcelona, Spain. 10-12/06/2013. DNA origami as potential hAGT recognition biosensor.

I. Haro. XXXIV Bienal de la Real Sociedad Española de Química. Simposium Química Biológica. Santander, Spain, 18/9/2013. "Citrullinated peptides in the diagnosis and prognosis of rheumatoid arthritis".

C. Solans. 5th International Symposium on Delivery of Functionality in Complex Food Systems (Haifa, Israel. 30/9/2013). Novel Self-Assemblies and Colloidal Structures for the Delivery of Food Actives.

C. Solans. 60 Sepawa Congress and European Detergents Conference (Fulda, Germany. 09/10/2013). Emulsification and Generation of Nano-emulsions by Low-energy Methods.

I. Alfonso. Instituto Universitario de Química Bio-Orgánica Antonio González, Universidad de la Laguna, Tenerife, Spain, Supramolecular Chemistry with Pseudopeptidic Structures.

J. Solà. Institut de Química Computacional i Catàlisi, Universitat de Girona, Girona, Spain. A short walk through Supramolecular Chemistry.

R. Crehuet. "Barcelona Biomed Conference: Frontiers in dynamics simulations of biological molecules", Barcelona, Spain, 10/2013.

R. Crehuet. Dynamo Workshop and Molecular dynamics simulations, Sao Paulo, Brasil, 10/2013.

L. Pérez, A. Pinazo. 104 AOCS Annual Meeting & Expo, 2013 Drug Delivery Systems based on diacyl arginine surfactants: preparation, characterization and evaluation of their biological activity.

Outreach activities organized at IQAC

IV Workshop CBN'12 ((Departament of Chemical and Biomolecular de Nanotecnology). 18 october 2012. Invited speakers:

1) Dr. Joan Salgado. Project Director of Gendiag. Translating molecular knowledge into clinical practice.

2) Dr. Pere Clapés. IQAC-CSIC. Synthetic opportunities and challenges of FSA aldolase in assymetric carbon-carbon bond formation.

3) Dr. Ramon Martínez Mañez. Institute of Applied Molecular Chemistry. University of Valencia. Gated mesoporous materials in delivery and sensing applications.

2012-2013. Participation of IQAC researchers in the Science week with 4-5 conferences to the general public related with the activities of the institute.

2012-2013. Participation of IQAC researchers in updating information directed to highschool teachers with 3 conferences related with the activities of the institute.

2012-2013. Participation of IQAC researchers courses of initiation to research on chemistry for highschool students.

2012. Celebration of the 70th anniversari of Porf. Joan Albaigés, 12 of November of 2012 with the presence of the president , vicepresident and institutional delegate of CSIC in Catalonia.

V Workshop CBN'13 (Departament of Chemical and Biomolecular de Nanotecnology). 17 october 2013. Invited speakers.

1) Dr. François Ganachaud. INSA-LYON. Drink it or use it? The "Ouzo effect" as a powerful tool to prepare aqueous nanodispersions of whatever solutes.

2) Dr. M. Rosa Infante. IQAC-CSIC. Sustainable Chemistry and Surfactans.

3) Dr. Oriol Ponsati. Desinenter Technologies. Trends to "nano" in Industrial Chemistry.

2013. Organization of a part of the 18th Conference dedicated to the memory of Dr. FÈLIX SERRATOSA.

Ph. D. Thesis

2012

20/04/2012
Alfred Fernández Castañé

Study of transport mechanisms involved in IPTG uptake by E. coli in high cell density cultures

Autonomous University of Barcelona
Supervisers: Gloria Caminal and Josep Lopez Santin

04/05/2012
Anna Carreras Cardona

A study of the Electron-Transfer properties of phenolics and their relationship with the biological activity on cancer cells

University of Barcelona
Supervisers: José Luis Torres, Lluis Julià and Marta Cascante

15/06/2012.
Leticia Fernández Arauzo
Péptidos sintéticos del GB virus C. Aplicación en el diagnóstico de infección y en el diseño de potenciales agentes terapéuticos contra el VIH-1

University of Barcelona
Supervisers: Isabel Haro and Maria José Gomara

26/06/2012
Marta Solé Carbonell
Statocyst sensory epithelia ultrastructural analysis of cephalopods exposed to noise

Universidad Politécnica de Catalunya, Centre Tecnològic de Vilanova i la Geltrú
Supervisors : Michel André, Carmen Quero, Manel López-Béjar

13/07/2012
Fátima Fernández Santos

Biosensores para la detección de antibióticos en matrices biológicas de interés en el sector agroalimentario

University of Barcelona
Supervisors: Mª Pilar Marco and Francisco Sanchez Baeza

13/07/2012
Rafael Gago Otero

Síntesis y actividad de nuevos antagonistas de feromona sexual de insectos plaga

University of Barcelona
Supervisors: Angel Guerrero and Mª Pilar Bosch

24/07/2012
Laia Rubio Toledano

Sistemes bicel•lars com a nova estratègia d'aplicació tòpica

University of Barcelona
Supervisors: Olga Serrano and José Luis Parra

25/07/2012
Susana Sánchez Tena

Caracterització de l'efecte de compostos naturals en models in vitro i in vivo de cáncer de colon

University of Barcelona
Supervisors: Jose Luis Torres, Marta Cascante and Pedro Vizán

28/09/2012
Javier Adrian Izquierdo

Novel Specific Receptor-based Techniques for Antibiotic Residue Analysis

University of Barcelona
Supervisors: Mª Pilar Marco and Francisco Sanchez Baeza.

24/10/2012.
Ruben Ferreira Aguilera

Els quàdruplex de guanina: estudis estructurals i diana farmacològica.

University of Barcelona
Supervisors: Ramon Eritja and Anna Aviñó

26/11/2012
Gelen Rodríguez Delgado

Efecto de los sistemas bicelares sobre la piel y su adecuación para la aplicación sobre otras dianas biológicas

University of Barcelona
Supervisors: Olga López and Mercedes Cócera

18/12/2012
Anna Alcaide López

A modular approach to sphingolipid analogs mediated by aziridines: synthesis and biological studies

University of Barcelona
Supervisors: Amadeu Llebaria

19/12/2012
Maria Garrido Martínez

New sphingolipid probes for metabolism and trafficking studies.

University of Barcelona
Supervisors: José Luís Abad and Antonio Delgado

13/07/2012
Carlos Rodríguez Rodríguez

Degradation of pharmaceuticals in sewage sludge by Trametes versicolor

Autonomous University of Barcelona
Supervisor: Gloria Caminal

30/04/2012
Manroshan Singh

Role of hydrophobically modified inulin on rubber latex stability and film formation

University of Barcelona
Supervisor: Jordi Esquena

2013

7/01/2013
Neus Vilanova García

Advanced emulsion formulations for the preparation of encapsulating systems University of Barcelona

Supervisors: Conxita Solans/Carlos Rodríguez

11/01/2013
Juan Antonio Mesa Díaz

Desarrollo de radicales libres estables solubles en agua y su aplicación al estudio de las transferencias electrónicas en células, tejidos y fluidos biológicos

University of Barcelona, 2013
Supervisors: Lluis Julià

30/01/2013
Alejandro Vílchez Villalba

Polymeric macroporous nanocomposites using highly concentrated emulsions as templates

University of Barcelona
Supervisors: Jordi Esquena and Carlos Rodríguez

31/01/2013
Kelly Pemartin

Inorganic nanoparticles synthesized by the novel oil-in-water microemulsion reaction method and their potential applications

University of Barcelona
Supervisors: Conxita Solans and Margarita Sánchez

1/02/2013
Camille Paulme

Design, characterization and applications of polyester nanoparticles obtained by enzymatic polymerization in nano-emulsions prepared by low-energy methods

University of Barcelona
Supervisors: Conxita Solans and Jordi Esquena

8/03/2013
Alda Lisa Concia

Chemoenzymatic synthesis of sugar-related polyhydroxylated compounds, iminocyclitols and their derivatives as glycosidase inhibitors.

University of Barcelona
Supervisor: Pere Clapés

26/06/2013
Miriam Corredor Sánchez

Chemical Modulation of Identified Hit Compounds as Apoptosis Inhibitors

University Ramon Llull
Supervisor: Àngel Messeguer

21/10/2013
Mònica Rosa

Disseny racional de lligands del receptor opioide i d'anàlegs d'opiorfina

University of Barcelona
Supervisors: Gregorio Valencia and Gemma Arsequell

20/11/2013
María Luisa Mateos Martín

Relación estructura/actividad de proantocianidinas procedentes de fuentes naturales de origen vegetal.

University of Barcelona, 2013
Supervisors: José Luis Torres and Elisabet Fuguet

25/11/2013
Nuria Tort Escribà

Desenvolupament d'una plataforma universal per a la multidetecció mitjançant la codificació espaial de cadenes d'ADN.

University of Barcelona
Supervisor: Mª Pilar Marco Colás

2/12/2013
Sonia Matas Moya

Reaccions adverses a penicil•lines: noves eines per a la prevenció i el diagnòstic

University of Barcelona
Supervisors: Roger Galve Bosch and Mª Pilar Marco Colás

5/12/2013
Olaia Fernández

Bioluminiscence imaging for the evaluation and development of new biomaterials for tissue engineering

University of Barcelona
Supervisor: Jerónimo Blanco

20/12/2013
Stefanie Leitner

Design of Multifunctional Polymeric Nanoparticles for Biomedical Applications

University of Barcelona
Supervisors: Conxita Solans, Mª José García Celma and Gabriela Calderó

Patent applications

2012

P201231137. Compuestos beta-lactámicos inhibidores de Apaf-1.

Á. Messeguer, I. Alfonso, M. Corredor, E. Pérez-Payá, M. Orzáez.

Priority date: 19/07/2012.

Applicant: Consejo Superior de Investigaciones Científicas (CSIC), Centro de Investigación Príncipe Felipe (CIPF).

2012. Priority patent Application Nº: ES201231137. Publication Nº: ES2443538

2013. PCT Application Nº: PCT/ES2013/070487. Publication Nº: WO2014013115.

P201230378 Compuestos derivados de doxiciclina como haptenos, conjugados y anticuerpos de los mismos, y método inmunoquímico para la detección de doxiciclina.

MP Marco Colás MP, J. Adrian, F. Sánchez Baeza.

Priority date: 13/03/2012

Applicant: Consejo Superior de Investigaciones Científicas (CSIC).

2012. Priority patent Application Nº: ES201230378.

2013. PCT Application Nº: PCT/ES2013/070155. Publication Nº: WO2013135930.

P201231836. Anticuerpos para la detección y cuantificación de agentes anticoagulantes.

JP Salvador; MP. Marco

Priority date: 27/11/2012

Applicant: Consejo Superior de Investigaciones Científicas (CSIC), Centro de Investigación en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN).

2012. Priority patent Application Nº: ES201231836. Publication Nº: ES2472290

2013. PCT Application Nº: PCT/ES2013/070816. Publication Nº: WO2014083226.

2013

P201330312. Haptenos y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por Pseudomonas aeruginosa.

MP Marco Colás, N. Pascual, C. Pastells, F. Sánchez Baeza, A. Villaverde, E. Rodríguez.

Priority date: 5/03/2013

Applicant: Consejo Superior de Investigaciones Científicas (CSIC), Centro de Investigación en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Universidad Autónoma de Barcelona (UAB).

2013. Priority patent Application Nº: ES201330312. Publication Nº: ES2504715

P201330939. Material compuesto adsorbente que comprende metales nobles y un polímero tensioactivo, procedimiento de síntesis y su utilización para la desulfuración de fluidos

R. Pons, J. Morros

Priority date: 21/06/2013

Applicant: Consejo Superior de Investigaciones Científicas (CSIC), Recursos Energéticos de Biomasa S.L (RENERBIO)

2013. Priority patent Application Nº: ES201330939

EP13382374. Glutamate receptor photomodulators

A. Llebaria, P. Gorostiza, X. Gómez, S. Pittolo, J. Giraldo, X. Rovira, C.Goudet, JP Pin

Priority date: 27/09/2013

Consejo Superior de Investigaciones Científicas (CSIC), Fundació Institut de Bioenginyeria de Catalunya (IBEC), Universidad Autónoma de Barcelona (UAB), Centre National de la Recherche Scientifique (CNRS)

2013. Priority patent Application Nº: EP13382374.

P201331587. Método de activación química superficial de un soporte sólido en base silicio mediante anclaje covalente directo de al menos una biomolécula de ácidos nucleicos

Bañuls MJ, Maquieira A, Eritja R, Escorihuela J, Grijalvo S, Puchades R. Priority date: 30/10/2013

Universidad Politécnica de Valencia (UPV), Consejo Superior de Investigaciones Científicas (CSIC), Centro de Investigación en Red en Bioingeniería, Biomateriales y Nanomedicina(CIBER-BBN)

2013. Priority patent Application Nº: ES201331587.

Licensed patents

2012

P201031622 Derivados de pequeños ARN de interferencia y su uso.

Licensor: Janus Developments (Spain)

P201031721 Haptenos e inmunoreactivos y su uso en la obtención de anticuerpos de familia e inmunoensayos para quinolonas.

Licensor: Unisensor (Belgium)

P201030298 Bicelas encapsuladas en liposomas y su aplicacion en sistemas diluidos

Licensors: SmartNano S.L. and Labiana S.L (Spain)

P200601933 Compound that can inhibit ubc13-uev interactions, pharmaceutical compositions and therapeutic uses

Licensor: TCD Pharma (Spain)

2013

P201031878 Eteres de hidroxitirosol

Licensor: BDF Ingredients (Spain)

Courses

Mª Pilar Marco. European Master in Quality in Analytical Laboratories. University of Algarve, Portugal, 2012.

Mª Pilar Marco. European Master in Quality in Analytical Laboratories. University of Barcelona. 2013.

Mª Pilar Marco. Ingeniería Biomédica y Aplicaciones del Electrónica. Universidad Autonoma de Barcelona. 2013.

Ramon Eritja. Genetic and celular basis of biotechnology. Master of Biotechnology. University of Barcelona, 2012 -2013.

Jordi Esquena. Course "Fenómenos Interfaciales en la Explotación de Yacimientos Petrolíferos" (Three editions: April 2012, Septembrer 2012 and June 2013), organized in collaboration with the University of Granada and the Group of Biocompatible Surfactants of the IQAC-CSIC.

Jordi Esquena. Practical tutorials of the "Master en Cosmética y Dermofarmacia" (Two editions: June-July 2012 and June-July 2013), in collaboration with "Centro de Estudios Superiores de la Industria Farmacéutica".

Conxita Solans. Organization of "Rheology of dispersions. Principles and applications" course, given by Prof. Tadros, 16-18 September 2013.

Isabel Haro. Coordinator of the Course: "Curso Experimental en Química Biológica, Ambiental y Tecnologías relacionadas" (Postgrado y Especialización del CSIC). 2012-2013.

José Luis Torres. Master of Biotecnología Molecular, University of Barcelona. 2012

Lluis Julià. Master of "Nanomaterials and Nanotechnology", University de Barcelona, 2012

Maria Teresa García. Aplicaciones industriales de los tensioactivos. Quimacova, 2013.

Lourdes Pérez. Fenómenos Interfaciales en la explotación de yacimientos petrolíferos, 17-21 Junio 2012, Barcelona,.

Lourdes Pérez. Fenómenos Interfaciales en la explotación de yacimeintos petrolíferos, 17-21 Junio 2013, Barcelona.

A. Manich. Estadística aplicada a la preformulación y formulación de medicamentos, dentro del Programa Título de Especialista (TEFIG) en Farmacia Industrial y Galénica. Curso de Postgrado, UB, 2012

A. Manich. Estadística, Planifiación de Experiencias y Análisis de Regresión. Curso de Formación, Laboratorios Esteve, 2012

A. Manich. Estadística aplicada a la preformulación y formulación de medicamentos, dentro del Programa Título de Especialista (TEFIG) en Farmacia Industrial y Galénica. Curso de Postgrado, UB, 2013

A. Manich. Introducción al diseño de experimentos. Cursos de Formación, 2013

A. Manich. Introducción al diseño de experimentos aplicado en la química. Cursos de Formación, 2013.

José Luis Parra. Organización del seminario: Usos y aplicaciones de la radiación Sincrotrón. Barcelona, Mayo 2012.

Participation in international graduate exchange programmes

Erasmus Programme- Staff Training. Professor Eyüp Sabah, Afyon Kocatepe University, 03200, Afyonkarahisar, Turkey. Coordination by Dr. Maria Teresa García. October 2013

UNIPHARMA/ Leonardo da Vinci Italian-Spanish bilateral exchanges. Coordination by Dr. Amadeu Llebaria. 2012-2013.

École National Superièure de Chimie de Lille. Université Chimie de Lille. Exchange Programme, 2012-2013

Media coverage

Multimedia presentation of the results obtained by "La Marató de TV3", XIII Symposium "La Marató de TV3: El dolor crònic" with the participation of 4 researchers of IQAC: Gregori Valencia, Gemma Arsequell, Amadeu Llebaria and Angel Messeguer (TV3, 27 June 2012, a las 21:50 pm).

Angel Guerrero. Las plagas del alcornoque. Digital journals Interempresas, 2013

(http://www.interempresas.net/Madera/Articulos/103993-Plagas-del-alcornoque.html, 2013)

Report on IQAC in the Spanish national radio. April 8, 2013 the programe "On the shoulder of giants ("A hombros del gigante") of RNE1 y RNE5, had a special programme dedicated to the description of the research activities of IQAC with description of the main activities and an interview to researchers of the institute.

05/03/2013. Press release on article published in Chem Eur. 19, 1920-1927 (2013) by Gómez-Pinto, I., Vengut-Climent, E., Lucas, R., Aviñó, A., Eritja, R., González, C., Morales, J.C. Comments in Diario Médico published 13/03/2013 and rdipress.com 05/03/2013.

18/07/2013. Press release on article published in Angew. Chem. Int. Ed. Engl., 52, 7747-7750 (2013) by Tintoré, M., Gállego, I., Manning, B., Eritja, R., Fàbrega, C. Comments in Diario Médico published 18/07/2013 and R + D CSIC 18/07/2013.

2

Department of Biological Chemistry and Molecular Modelling

Department of Biological Chemistry and Molecular Modelling

Head: Jesús Joglar Tamargo

Research interests of this Department are focused on:

- Molecules of biological and biomedical interest. Isolation, design, synthesis, biosynthesis, and activity evaluation of drugs, insect pheromones, secondary metabolites, enzymatic inhibitors, biocatalysts, agro-forestry byproducts and antioxidants.
- Molecular recognition of ions and molecules of biological interest.
- Study of non covalent interactions. Modelling of enzymatic catalysis mechanisms.
- Modification of the activity and selectivity of bio-catalysts by means of genetic engineering. Mecha-nisms of action of antioxidant protectors.
- Biorational control of plagues. Characterization of insect proteins by means of proteomic and molec-ular biology techniques.
- Persistent organic free radicals as biochemical sensors.
- Study of the electronic structure and reactivity of molecules by means of theoretical chemistry com-putational techniques. Computational elucidation of reaction mechanisms of interest in atmospheric chemistry. New theoretical methods for exploring potential energy surfaces.

Research groups

- Nutraceuticals and Free Radicals
- Biotransformation and Bioactive Molecules
- Supramolecular Chemistry
- Ecological Chemistry
- Theoretical and Computational Chemistry
- Bioorganic Chemistry
- Biologically Active Phytochemicals

Nutraceuticals and Free Radicals

Research at NFR involves the thorough evaluation of potentially new disease preventing and health promoting agents such as nutraceuticals or functional food components. The nutraceuticals (e.g. antioxidant polyphenols, omega-3 polyunsaturated fatty acids, iminosugars) are natural products obtained by either from agricultural and fishery by-products or by environmentally friendly biosynthetic procedures. The biological activities tested on the nutraceuticals are related to the control of the oxidative stress which is a major damaging process, mediated by free radicals and occurring in many disorders (metabolic syndrome, cardiovascular disease, type 2 diabetes, cancer, Alzheimer, Parkinson). The study of free radicals, their reactivity, their use as probes for antioxidant activity and their control or elimination by natural nutraceuticals is a central focus of our research. Recently, we have focused on in vivo studies with rats models of the metabolic syndrome and tested combinations of nutraceuticals with complementary activities. New water soluble radical probes to be used in biological fluids have been developed. The antioxidant activity is measured by Electron Paramagnetic Resonance spectroscopy with the spin trapping and radical scavenging methodology.

STAFF

LUIS JULIÀ BARGÈS, GROUP LEADER
JOSEP LLUÍS TORRES SIMON
LLUÍS FAJARÍ AGUDO

Ph. D.

JARA PÉREZ JIMÉNEZ
SARA RAMOS ROMERO

Ph. D. STUDENTS

ANNA CARRERAS CARDONA
JOSÉ ANTONIO MESA
EUNICE MOLINAR

Publications (articles)

Antioxidant dietary fibre (ADF) in lipid rich fruits: Adapted methodology for quantification and characterization.

M.S.M. Rufino, R.E. Alves, E.S. Brito, M. Tabernero, J. Pérez-Jiménez, F. Saura-Calixto

Acta Horticulturae, 939, 263-267, 2012

Effects of temperature and time on polyphenolic content and antioxidant activity in the pressurized hot water extraction of deodorized thyme (Thymus vulgaris).

Vergara-Salinas JR, Pérez-Jiménez, J, Torres JL, Agosin E, Pérez-Correa JR.

J. Agric. Food Chem., 60, 10920-10929, 2012

Selective control of the radical-scavenging activity of poly(phenols) in aqueous media in terms of their electron-donor properties, using a stable organic radical as chemical sensor.

Mesa JA, Torres JL, Juliá L.

Talanta, 101, 141-147, 2012

Analysis of proanthocyanidins in almond blanch water by HPLC–ESI–QqQ–MS/MS and MALDI–TOF/TOF MS.

Pérez-Jiménez, J, Torres, J.L.

Food Res Int, 49, 798–806, 2012

Grape epicatechin conjugates prevent erythrocyte membrane protein oxidation.

Martínez V, Ugartondo V, Vinardell MP, Torres JL, Mitjans M.

J. Agric. Food Chem., 60, 4090–4095, 2012

Antioxidant mechanism of grape procyanidins in muscle tissues: Redox interactions with endogenous ascorbic acid and α-tocopherol.

Iglesias J, Pazos M, Torres JL, Medina I.

Food Chemistry, 134, 1767-1774, 2012

Profile of urinary and fecal proanthocyanidin metabolites from common cinnamon (Cinnamomum zeylanicum L.) in rats.

Mateos-Martín ML, Pérez-Jiménez J, Fuguet E, Torres JL.

Mol. Nutr. Food Res., 56, 1–5, 2012

Inhibition of deleterious chronic wound enzymes with plant polyphenols.

Díaz-González M, Rocasalbas G, Francesko A, Touriño S, Torres JL, Tzanov T.

Biocat. Biotrans., 30, 102-110, 2012

Punicalagin and catechins contain polyphenolic substructures that influence cell viability and can be monitored by radical chemosensors sensitive to electron transfer.

Carreras A, Mateos-Martín ML, Velázquez-Palenzuela A, Brillas E, Cascante M, Juliá L, Torres JL.

J. Agric. Food Chem. 60, 1659–1665, 2012

Hamamelitannin from witch hazel (Hamamelis virginiana) displays specific cytotoxic activity against colon cancer cells.

Sánchez-Tena S, Fernández-Cachón ML, Carreras A, Mateos-Martín ML, Costoya N, Moyer MP, Núñez MJ, Torres JL, Cascante M.

J. Nat. Prod. 76, 26-33, 2012

Determination of D-fagomine in buckwheat and mulberry by cation exchange HPLC/ESI–Q-MS.

Amézqueta S, Galán E, Fuguet E, Carrascal M, Abián J, Torres JL.

Anal. Bioanal. Chem. 402, 1953–1960, 2012

Preparation and characterization of persistent maltose-conjugated triphenylmethyl radicals.

Mesa JA, Velázquez Palenzuela A, Brillas E, Coll J, Torres JL, Juliá L.

J. Org. Chem. 77(2) 1081-1086, 2012.

A polyphenol-enriched cocoa extract reduces free radicals produced by mycotoxins.

Corcuera L, Amézqueta S, Arbillaga L, Vettorazzi A, Touriño S, Torres JL, López de Cerain A.

Food Chem Toxicol, 50, 989–995, 2012

New identification of proanthocyanidins in cinnamon (Cinnamomum zeylanicum L.) using MALDI-TOF/TOF mass spectrometry.

Mateos-Martín ML, Fuguet E, Quero C, Pérez-Jiménez J, Torres JL.

Anal Bioanal Chem. 402, 1327–1336, 2012

Non-extractable proanthocyanidins from grapes are a source of bioavailable (epi)catechin and derived metabolites in rats.

Mateos-Martín ML, Pérez-Jiménez J, Fuguet E, Torres JL.

Brt. J.Nutr., 108, 290-297, 2012

D-Fagomine lowers postprandial blood glucose and modulates bacterial adhesion.

Gómez L, Molinar-Toribio E, Calvo-Torras MA, Adelantado C, Juan ME, Planas JM, Cañas X, Lozano C, Pumarola S, Clapés P, Torres JL.

Brt. J. Nutr., 107, 1739–1746, 2012

Protective effect of the omega-3 polyunsaturated fatty acids: Eicosapentaenoic acid/Docosahexaenoic acid 1:1 ratio on cardiovascular disease risk markers in rats.

Lluís L, Taltavull N, Muñoz-Cortés M, Sánchez-Martos V, Romeu M, Giralt M, Molinar-Toribio E, Torres JL, Pérez-Jiménez J, Pazos M, Méndez L, Gallardo JM, Medina I, Nogués MR.

Lipids in Health & Disease, 12, 140, 2013

Phenol-Explorer 3.0: a major update of the Phenol-Explorer database to incorporate data on the effects of food processing on polyphenol content.

Rothwell JA, Perez-Jimenez J, Neveu V, Medina-Remón A, M'Hiri N, García-Lobato P, Manach C, Knox C, Eisner R, Wishart DS, Scalbert A

Database 2013: bat070, 2013.

Effect of pressurized hot water extraction on antioxidants from grape pomace before and after enological fermentation.

Vergara-Salinas JR, Bulnes P, Zúñiga MC, Pérez-Jiménez J, Torres JL, Mateos-Martín ML, Agosin E, Pérez-Correa, JR.

J. Agric. Food Chem., 61(28), 6929–6936, 2013

Grape antioxidant dietary fiber inhibits intestinal polyposis in ApcMin/+ mice: relation to cell cycle and immune response.

Sánchez-Tena S, Lizárraga D, Miranda A, Vinardell MP, García-García F, Dopazo J, Torres JL, Saura-Calixto F, Capellà G, Cascante M.

Carcinogenesis, 34(8), 1881–1888, 2013

A tri(potassium sulfonate) derivative of perchlorotriphenylmethyl radical (PTM) as a stable water soluble radical-scavenger of the hydroxyl radical more powerful than 5,5-dimethyl-1-pyrroline-N-oxide.

Mesa JA, Chávez S, Fajarí L, Torres JL, Juliá L.

RSC Adv. 3 9949-9956, 2013.

Epicatechin gallate impairs colon cancer cell metabolic productivity.

Sánchez-Tena S, Alcarraz-Vizán G, Silvia Marin S, Torres JL, Cascante M.

J. Agric. Food Chem., 61(18), 4310–4317, 2013

High electron transfer capacity of thio-derivatives of tea catechins measured using a water soluble stable free radical and their effects on colon cancer cells.

Carreras A, Mesa JA, Cascante M, Torres JL, Juliá L.

New J. Chem., 37, 2043-2050, 2013.

Dietary intake and major food sources of polyphenols in a Spanish population at high cardiovascular risk: The PREDIMED study.

Tresserra-Rimbau A, Medina-Remón A, Pérez-Jiménez J, Martínez-González MA, Covas MI, Corella D, Salas-Salvadó J, Gómez-Gracia E, Lapetra J, Arós F, Fiol M, Ros E, Serra-Majem L, Pintó X, Muñoz MA, Saez GT Ruiz-Gutiérrez V, Warnberg J, Estruch R, Lamuela-Raventós RM.

Nutrition, Metabolism Cardiovascular Dis, 23, 953-959, 2013

The presence of D-fagomine in the human diet from buckwheat-based foodstuffs.

Amézqueta S, Galán E, Vila-Fernández I, Pumarola S, Carrascal M, Abian J, Ribas-Barba L, Serra-Majem L, Torres JL.

Food Chem, 136, 1316–1321, 2013

A new approach to produce plant antioxidant-loaded chitosan for modulating proteolytic environment and bacterial growth.

Rocasalbas G, Touriño S, Torres JL, Tzanov T.

J. Mater. Chem. B, 1, 1241-1248, 2013

Mexican 'Ataulfo' mango (Mangifera indica L) as a source of hydrolyzable tannins. Analysis by MALDI-TOF/TOF MS.

Sáyago-Ayerdi SG, Moreno-Hernández CL, Montalvo-González E, García-Magaña ML, Mata-Montes de Oca M, Torres JL, Pérez-Jiménez J.

Food Res Int, 51, 188–194, 2013

Reduced protein oxidation in Wistar rats supplemented with marine ω3 PUFAs.

Méndez L, Pazos M, Gallardo JM, Torres JL, Pérez-Jiménez J, Nogués R, Romeu M, Medina I.

Free Radical Biol Med, 55, 8-20, 2013

Research Projects

Desarrollo aplicaciones de análogos de azucares: D-fagomina. Estudios de actividad, eficacia y toxicidad en su uso como nuevo ingrediente nutricional para la prevención de sobrepeso y resistencia a enfermedades.

Nacional, IPT-2011-0828-900000

2011-2014

Nuevos agentes antivirales con estructuras fenólicas atípicas

Internacional, 2010CR0011

2011-2012

Mecanismo de acción de los ácidos grasos poliinsaturados de origen marino en el síndrome metabólico y sinergismo con polifenoles e iminociclitoles

Nacional, AGL2009-12374-C03-03

2010-2013

Desarrollo de procesos para la generación de sustancias a partir de procedimientos limpios(green and white biotechnologies), su análisis y su valoración biológica. Internacional, aldoright, programa eurotransbio, ETB-2010-35

2011-2012

Microreactor technology for continuous enzymatic reactions catalyzed by C-C-bond forming enzymes (MicroTechEnz).

Internacional, ERA-IB Mod. A, PIM2010EEI-00607

2011-2014

Research highlights

A tri(potassium sulfonate) derivative of perchlorotriphenylmethyl radical (PTM) as a stable water soluble radical-scavenger of the hydroxyl radical more powerful than 5,5-dimethyl-1-pyrroline-N-oxide.J. A. Mesa, S. Chávez, L. Fajarí, J.L. Torres, L. Juliá

RSC Advances, 3, 9949-9956 (2013) (A) doi: 10.1039/c3ra41499j.

The tripotassium salt of tris(2,3,5,6-tetrachloro-4-hydroxysulfonylphenyl)methyl radical (3 K+ TSPTM3-) reacts in water with hydroxyl radical very fast with a rate constant (k = 2.4 [times] 1011 M-1 s-1) much higher than that of the reaction of hydroxyl radical with the spin trap 5,5-dimethyl-1-pyrroline-N-oxide (DMPO) (k = 3.4 [times] 109 M-1 s-1). The reaction affects the radical character of the molecule and is monitored by electron paramagnetic resonance (EPR). The hydroxyl radical scavenging is established by the characterization of the resulting water-soluble product as the dipotassium salt of 4-[bis(2,3,5,6-tetrachloro-4-hydroxysulfonylphenyl)methylene]-2,3,5,6-tetrachlorocyclohexa-2,5-dien-1-one (2). This new radical can be used for the evaluation of the presence of the putatively damaging hydroxyl radical in plasma and urine.

D-Fagomine lowers postprandial blood glucose and modulates bacterial adhesion

L. Gómez, E. Molinar-Toribio, M. A. Calvo-Torras, C. Adelantado, M. E. Juan, J. M. Planas, X. Cañas, C. Lozano, S. Pumarola, P. Clapés, J. L. Torres

Brt. J. Nutr. 172, 1739-1746 (2012) doi:10.1017/S0007114511005009.

D-Fagomine is an iminosugar originally isolated from seeds of buckwheat (Fagopyrum sculentum Moench). We tested D-fagomine for activities connected to a reduction in the risk of developing insulin resistance, becoming overweight and suffering from an excess of potentially pathogenic bacteria. The activities were: intestinal sucrose inhibition in vitro, modulation of postprandial blood glucose in rats, bacterial agglutination and bacterial adhesion to pig intestinal mucosa. When ingested together with sucrose or starch, D-fagomine lowered blood glucose in a dose-dependent manner without stimulating insulin secretion. Moreover, D-fagomine (0•14mM) agglutinated 60% of Enterobacteriaceae (Escherichia coli, Salmonella enterica serovar Typhimurium) populations (P<0•01), while it did not show this effect on Bifidobacterium spp. or Lactobacillus spp. At the same concentration, D-fagomine significantly (P<0•001) inhibited the adhesion of Enterobacteriaceae (95–99% cells in the supernatant) and promoted the adhesion of Lactobacillus acidophilus (56% cells in the supernatant) to intestinal mucosa. Based on all this evidence, D-fagomine may be used as a dietary ingredient or functional food component to reduce the health risks associated with an excessive intake of fast-digestible carbohydrates, or an excess of potentially pathogenic bacteria.

Biotransformation and Bioactive Molecules

The research is focused on the design, production and evaluation of biocatalysts and biologically active molecules. Chemoenzymatic methodology has the potential to access stereochemically complex molecules that are not produced easily by conventional organic synthesis. Hence, they are particularly appropriate for obtaining new types of structures (i.e. generate molecular diversity) accessible for investigations in drug discovery. A fundamental component of the chemoenzymatic methodology is the biocatalysts. The research focus includes computational models for ligand-protein interaction as a way to redesign or rationally modify the biocatalysts and the biologically active molecules.

STAFF

PEDRO CLAPES SABORIT, GROUP LEADER
JORGE BUJONS VILÀS
GLORIA CAMINAL SAPERAS (Service Commission UAB)
JESUS JOGLAR TAMARGO

Ph. D. STUDENTS

ALDA LISA CONCIA
LIVIA GÓMEZ CORTÉS
ARISTOTELIS KOTRONOULAS
ANNA SZEKRENYI
KAREL HERNANDEZ SANCHEZ
ANNA SOLER CASAPONSA
RAQUEL ROLDÁN
CARLOS RODRÍGUEZ RODRÍGUEZ
BRUNO ALMEIDA COTRIM
XAVIER GARRABOU PI
MARIANA GUTIERREZ TEJEDA

Publications (articles)

Hydrogen peroxide in biocatalysis. A dangerous liaison.

Hernandez K, Berenguer-Murcia A, Rodrigues RC, Fernandez-Lafuente R.

Curr Org Chem, 16(22), 2652-2672, 2012

Bioaugmentation of sewage sludge with Trametes versicolor in solid-phase biopiles produces degradation of pharmaceuticals and affects microbial communities.

Rodríguez-Rodríguez CE, Jagger A, Pereira MA, Sousa DZ, Petrovic M, Alves MM, Barceló D, Caminal G, Vicent T.

Environ. Sci. Technol., 46, 12012-12020, 2012

Removal of pharmaceuticals, polybrominated flame retardants and UV-filters from sludge by the fungus Trametes versicolor in bioslurry reactor.

Rodríguez-Rodríguez CE, Barón E, Gago-Ferrero P, Jeli, A, Llorca M, Farré M, Díaz-Cruz MS, Eljarrat E, Petrovic M, Caminal G, Barceló D, Vicent T.

J Hazard Mat, 233-4, 235– 243, 2012

Chemoenzymatic synthesis, structural study and biological activity of novel indolizidine and quinolizidine iminocyclitols.

Gómez L, Garrabou X, Joglar J, Bujons J, Parella T, Vilaplana C, Cardona PJ, Clapés P.

Org. Biomol. Chem., 10, 6309–6321, 2012

Direct measurements of IPTG enable analysis of the induction behavior of E. coli in high cell density cultures.

Fernández-Castané A, Caminal G, López-Santín, J.
Microbial Cell Factories 11, 58, 2012

Evaluation of fungal- and photo-degradation as potential treatments for the removal of sunscreens BP3 and BP1.

Gago-Ferrero P, Badia-Fabregat M, Olivares A, Piña B, Blánquez P, Vicent T, Caminal G, Díaz-Cruz MS, Barceló D.

Sci Total Environ, 427–428, 355–363, 2012

Degradation of UV filters in sewage sludge and 4-MBC in liquid medium by the ligninolytic fungus Trametes versicolor.

Badia-Fabregat M, Rodríguez-Rodríguez CE, Gago-Ferrero P, Olivares A, Piña B, Díaz-Cruz MS, Vicent T, Barceló D, Caminal G.

J Environ Manag 104, 114-120, 2012

Effects of MDMA (ecstasy) and two of its metabolites on rat embryos in vitro.

Barenys M, Flick B, Boix N, Almeida B, Joglar J, Klug S, Llobet JM.

Reprod. Toxicol., 34, 57-65, 2012

In situ aldehyde generation for aldol addition reactions catalyzed by d-fructose-6-phosphate aldolase.

Mifsud M, Szekrényi A, Joglar J, Clapés P.

J Mol Cat B: Enzymatic, 84, 102-107, 2012

Continuous degradation of a mixture of sulfonamides by Trametes versicolor and identification of metabolites from sulfapyridine and sulfathiazole.

Rodríguez-Rodríguez CE, García-Galán J, Blánquez P, Díaz-Cruz MS, Barceló D, Caminal G, Vicent, T.

J Hazard Mat, 213– 214, 347– 354, 2012

A comparative life cycle assessment of two treatment technologies for the Grey Lanaset G textile dye: Biodegradation by Trametes versicolor and granular activated carbon adsorption

Gabarrell, X.; Font, M.; Vicent, T.; Caminal, G.; Sarrà, M.; Blánquez, P.

Int J Life Cycle Assessment, 17, 613- 624, 2012

Unsaturated fatty alcohol derivatives of olive oil phenolic compounds with potential low-density lipoprotein (LDL) antioxidant and antiobesity properties.

Cotrim BA, Joglar J, Rojas MJL, Del Olmo JMD, Macías-González M, Cuevas MR, Fitó M, Muñoz-Aguayo D, Covas Planells MI, Farré M, Rodríguez De Fonseca F, De La Torre R.

J Agric Food Chem. 60, 1067−1074, 2012

Evidencing the role of lactose permease in IPTG uptake by Escherichia coli in fed-batch high cell density cultures.

Fernández-Castané A, Vine CE, Caminal G, López-Santín J.

J Bacteriol. 157, 391-398, 2012

D-Fagomine lowers postprandial blood glucose and modulates bacterial adhesion.

Gómez L, Molinar-Toribio E, Calvo-Torras MA, Adelantado C, Juan ME, Planas JM, Cañas X, Lozano C, Pumarola S, Clapés P, Torres JL.

Brit J Nutr., 107, 1739–1746, 2012

Optimisation of the operational conditions of trichloroethylene degradation using Trametes versicolor under quinone redox cycling conditions using central composite design methodology.

Vilaplana M, García AB, Caminal G, Guillén, F, Sarrà M.

Biodegradation 23(2), 333-341, 2012

Effects of MDMA (ecstasy) and two of its metabolites on rat embryos in vitro.

Barenys M, Flick B, Boix N, Almeida B, Joglar J, Klug S, Llobet JM

Reprod. Toxicol. 34, 57-65, 2012

Dose-dependent metabolic disposition of hydroxytyrosol and formation of mercapturates in rats.

Kotronoulas A, Pizarro N, Serra A, Robledo P, Joglar J, Rubió L, Hernaéz Á, Tormos C, Motilva MJ, Fitó M, Covas M-I, Solà R, Farré M, Saez G, De La Torre R.

Pharm Res, 77, 47–56, 2013

Fungal permeable reactive barrier to remediate groundwater in an artificial aquifer.

Folch A, Vilaplana M, Amado L, Vicent T, Caminal G.

J Hazard Mat, 262, 554–560, 2013

Mathematical model for aldol addition catalyzed by two d-fructose-6-phosphate aldolases variants overexpressed in E. Coli.

Sudar M, Findrik Z, Vasić-Rački D, Clapés P, Lozano C

J Biotech, 167(3), 191– 200, 2013

Optimizing the control of apoptosis by amide/triazole isosteric substitution in a constrained peptoid.

Corredor M, Bujons J, Orzáez M, Sancho M, Pérez-Payá E, Alfonso I, Messeguer A.

Eur J Med Chem., 63, 892-896, 2013.

Aldol addition of dihydroxyacetone to N-Cbz-3-aminopropanal catalyzed by two aldolases variants in microreactors.

Sudar M, Findrik Z, Vasić-Rački D, Clapés P, Lozano C.

Enzyme Microb Technol, 53(1), 38-45, 2013

Allopregnanolone and pregnanolone analogues modified in the C ring: Synthesis and activity.

Slavíková B, Bujons J, Matyáš L, Vidal M, Babot Z, Krištofíková Z, Suñol C, Kasal A

J. Med. Chem., 56(6), 2323-2336, 2013

Chemo-enzymatic synthesis and glycosidase inhibitory properties of DAB and LAB derivatives.

Concia AL, Gómez L, Bujons J, Parella T, Vilaplana C, Cardona PJ, Joglar J, Clapés P.

Org. Biomol. Chem., 11(12), 2005-2021, 2013

Syntheses of dipeptide alcohols and dipeptide aldehyde precursors catalyzed by plant cysteine peptidases.

Morcelle SR, Cánepa AS, Padró JM, Llerena-Suster CR, Clapés P.

J Mol Cat B: Enzymatic, 89, 130–136, 2013

Co-composting as a management strategy to reuse the white-rot fungus Trametes versicolor after its use in a biotechnological process.

Marco E, Font X, Sánchez A, Gea T, Gabarrell X, Caminal G. Int. J. Environ Waste Management, 11(1), 100 - 108, 2013

Detection, synthesis and characterization of metabolites of steroid hormones conjugated with cysteine.

Fabregat A, Kotronoulas A, Marcos J, Joglar J, Alfonso I, Segura J, Ventura R, Pozo OJ.

Steroids, 78(3), 327–336, 2013

15N NMR Spectroscopic and theoretical GIAO-DFT studies for the unambiguous characterization of disubstituted 1,2,3-triazoles.

Corredor, M., Bujons, J., Messeguer, A., Alfonso, I.

Org. Biomol. Chem. 11, 7318-7325, 2013

Fungal permeable reactive barrier to remediate groundwater in an artificial aquifer

Albert Folch; Marcel Vilaplana; Leila Amado; Teresa Vicent; Gloria Caminal.

.Journal of Hazardous Materials. 262, pp. 554 – 560, 2013.

Publications
(books and book chapters)

Carbon–Carbon Bond-Forming Enzymes for the Synthesis of Non-natural Amino Acids.

Clapés P., Joglar, J., Gutierrez, M.

Methods in Molecular Biology 794, 73-85. Springer Science+Business Media, LLC, 2012.

Enzyme-Catalyzed Aldol Additions.

P. Clapés and J. Joglar.

Modern Methods in Stereoselective Aldol Reactions. Rainer Mahrwald, Ed. Wiley-VCH Verlag GmbH, 2013

Emerging Organic Contaminants in sludges. In The Handbook of Environmental Chemistry, V.24.

Vicent T, Caminal, G.; Eljarrat, E.; Barceló, D. (Eds). Springer-Verlag, Heidelberg Germany. 2013

Biodegradation of pharmaceuticals by fungi and metabolites identification. C. Cruz-Morató CE, Rodríguez E, Marco-Urrea M, Sarrà M, Caminal G, Vicent T, Jelic A, Gracía-Galán MJ, S. Pérez S, Díaz-Cruz, MS, Petrovic M, Barceló D.

UV filters biodegradation by fungi, metabolites identification and biological activity assessment.

Badia-Fabregat M, Caminal G, Vicent T, Blánquez P, Gago-Ferrero P, Olivares A, Piña B, Díaz-Cruz MS, Barceló D. In Emerging Organic Contaminants in sludges. In The Handbook of Environmental Chemistry, V.24. Vicent T; Caminal G, Eljarrat E, Barceló D. (Eds). Springer-Verlag, Heidelberg, Germany. 2013

Biodegradation of technical products of brominated flame retardant by fungi.

Vilaplana M, Caminal G, Serrà M, Barón E, Gorga M, Thienpont B, D. Raldúa D, E. Eljarrat E, Barceló B.

In Emerging Organic Contaminants in sludges. In The Handbook of Environmental Chemistry, V.24. Vicent, T.; Caminal, G.; Eljarrat, E.; Barceló, D. (Eds). Springer-Verlag, Heidelberg, Germany. 2013

Fungal-Mediated Degradation of Emerging Pollutants in Sewage Sludge.

Rodríguez-Rodríguez CE, Caminal G, Vicent T, Díaz-Cruz MS, Eljarrat E, Farré M, López de Alda MJ, Petrovic M, Barceló D.

In Emerging Organic Contaminants in sludges. In The Handbook of Environmental Chemistry, V.24. Vicent T, Caminal G, Eljarrat E, Barceló D. (Eds). Springer-Verlag, Heidelberg, Germany. 2013

Research Projects

Aproximación hacia un control de plagas de insectos de Rediseño de carboligasas para la formación asimétrica de enlaces carbono-carbono: hacia la síntesis one-pot multietapa de compuestos polioxigenados

Nacional, CTQ2012-31605

2013-2015

Synthesis of recently reported phase ii metabolites for their inclusion in routine doping control

Internacional, WADA-12A130P

2013-2014

Tecnología de microrreactores para reacciones enzimáticas de formación de enlaces carbono-carbono.

Nacional, PIM2010EEI-00607

2011-2014

Síntesis enzimática de aminoácidos no proteinogénicos para conjugaciones bioortogonales

Nacional, AIB2010DE-00405

2011-2012

Estrategias quimo-enzimáticas para la síntesis orientada a la diversidad. Adiciones aldólicas biocatalíticas en cascada para la preparación de nuevos productos bioactivos

Nacional, CTQ2009-07359

2010-2013

Desarrollo de procesos para la generación de sustancias a partir de procedimientos limpios(green and white biotechnologies), su análisis y su valoración biológica. proy. aldoright del programa eurotransbio

2011-2012

Preparacion y evaluacion de inhibidores de colina quinasa con potencial actividad antitumoral

Nacional, petri: pet2008_0312

2010-2011

Desarrollo del proceso y aplicaciones en relacion con la patente "chemoenzymatic process for the preparation of iminocyclitols"

2009-2010

Procesos para la generacion de sustancias a partir de procedimientos limpios /white biotechnology), su analisis y valoracion biologica

2008-2010

Red biotecnologia de materiales lignocelulosicos: retos moleculares, enzimaticos y quimicos. para su aplicacion industrial y medioambiental

Nacional, BIO2009-07866-E

2010-2012

Nuevas alternativas para la producción microbiana de enzimas y síntesis multienzimática estereoselectiva

Nacional MICINN CTQ 2011-28398-C02-01

2012-2014

Implementing an Enzyme Engineering Technology Platform for the provision of tailor-made enzymes to biocatalytic synthesis" (Eng Biocat). ERA-IB

MICINN. Programa Nacional de Internacionalización de la I+D. EUI2008-03615

2009- 2012

Estudios de procesos de dihaloeliminación en sedimentos marinos y de agua dulce para su aplicación en biorremedicación

Autonomous University of Barcelona

2011-2013

Biotratamiento y estructura de la comunidad microbiana de residuos sólidos

urbanos y lodos de EDAR

Nacional MICINN- SG de Programas Internacionales: AIB 2010PT-00169

2011-2013

Tratamiento no convencional de degradación por hongos de fármacos en efluentes: desarrollo de proceso, monitorización y evaluación del riesgo

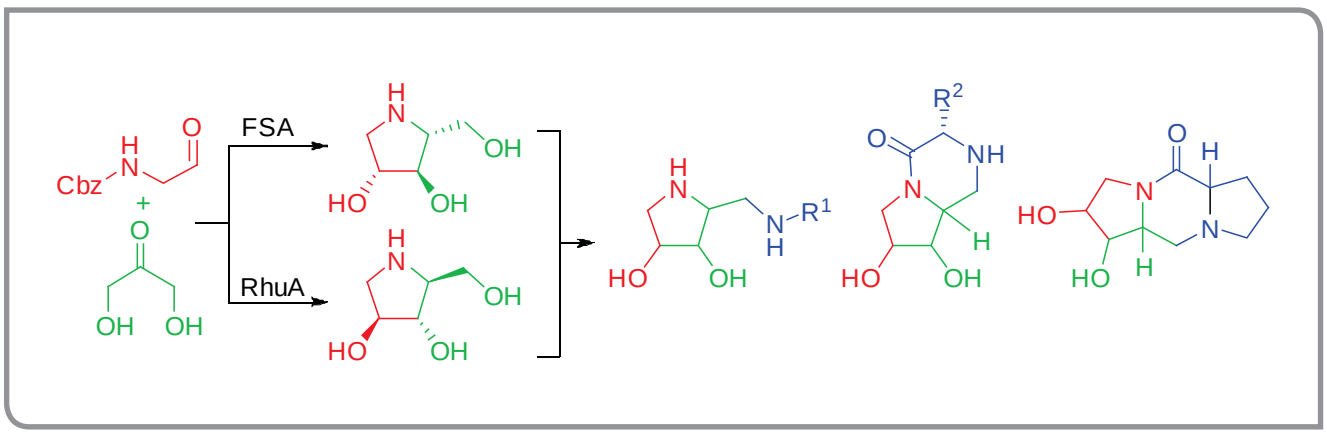
Nacional, MICINN, CTQ 2010-21776-C02-01

2010-2013

Research highlights

The best results obtained in 2012-2013 are:

- An efficient chemo-enzymatic methodology for the synthesis, conformational study and inhibitory properties of diverse indolizidine and quinolizidine iminocyclitols.
- Chemo-enzymatic synthesis and glycosidase inhibitory properties of DAB and LAB derivatives.
- One-pot multistep enzymatic oxidation-aldol addition reactions catalyzed by laccase/O2/2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO) system and D-fructose-6-phosphate aldolase variants.
- Biocatalytic aldol addition reactions catalyzed by D-fructose-6-phosphate aldolase variants in microreactors.



Supramolecular Chemistry

Supramolecular chemistry is the "chemistry beyond the molecule" and deals with the interactions between chemical species in an ordered and hierarchical way, leading to the formation of well-defined supramolecules. We mainly work in the fields of molecular recognition, programmed folding and self-assembling processes, using a large variety of experimental and theoretical approaches. The discovery, preparation and study of new synthetic receptors for biologically interesting molecules and ions (especially anions) are our main activities. We also use supramolecular approaches to synthetic procedures, such as templated synthesis, dynamic combinatorial chemistry and constitutional dynamic chemistry. Additionally, we collaborate with several groups (both at IQAC and outside) to study biomolecular and biomimetic systems from a supramolecular point of view.

STAFF

IGNACIO ALFONSO RODRIGUEZ

Ph. D.

CIRIL JIMENO MOLLET
JORDI SOLA I OLLER
ENRICO FAGGI
ANGEL MANUEL VALDIVIELSO PABLO

Ph. D. STUDENT

JOAN ATCHER UBIERGO
INCI GUNLER
MARIA LAFUENTE FABRA
ANNA SERRA PONT

Publications (articles)

Tuning chloride binding, encapsulation, and transport by peripheral substitution of pseudopeptidic tripodal small cages.

Martí I, Rubio J, Bolte M, Burguete MI, Vicent C, Quesada R, Alfonso I, Luis SV.

Chem. Eur. J. , 18, 16728-16741, 2012

Studies on the amination of aryl chlorides with a monoligated palladium catalyst: kinetic evidence for a cooperative mechanism.

Jimeno C, Christmann U, Escudero-Adán EC, Vilar R, Pericàs MA.

Chem. Eur. J., 18, 16510-16516, 2012.

Conformational analysis of a model synthetic prodiginine.

García-Valverde M, Alfonso I, Quiñonero D, Quesada R.

J. Org. Chem., 77, 6538–6544, 2012

Efficient synthesis of pseudopeptidic molecular cages.

Moure A, Luis SV, Alfonso I.

Chem. Eur. J., 18, 5496-5500, 2012

Interplay between hydrophilic and hydrophobic interactions in the self-assembly of a gemini amphiphilic pseudopeptide: from nano-spheres to hydrogels.

Rubio J, Alfonso I, Burguete MI, Luis SV.

Chem. Commun., 48, 2210–2212, 2012

The effect of DMSO in the aqueous thiol–disulphide dynamic covalent chemistry of model pseudopeptides.

Atcher J, Alfonso I.

RSC Adv, 3, 25605-25608, 2013

15N NMR spectroscopic and theoretical GIAO-DFT studies for the unambiguous characterization of disubstituted 1,2,3-triazoles.

Corredor M, Bujons J, Messeguer À, Alfonso I.
Org Biomol Chem.11, 7318-7325, 2013

Biological activity of synthetic ionophores: ion transporters as prospective drugs?.

Alfonso I, Quesada R.

Chem. Sci., 4, 3009-3019, 2013

Minimalistic amino amides as models to study N–H...π interactions and their implication in the side chain folding of pseudopeptidic molecules.

Faggi E, Luis SV, Alfonso I.

RSC Adv., 3, 11556-11565, 2013

TiO2(SiO2)x and ZrO2(SiO2)x Cryogels as catalysts for the citronellal cyclization to isopulegol .

Jimeno C, Miras J, Esquena, J.

Catalysis Letters, 143, 616-623, 2013

Optimizing the control of apoptosis by amide/triazole isosteric substitution in a constrained peptoid.

Corredor M, Bujons J, Orzáez M, Sancho M, Pérez-Payá E, Alfonso I, Messeguer A.

Eur J Med Chem. 63, 892-896, 2013

Detection, synthesis and characterization of metabolites of steroid hormones conjugated with cysteine.

Fabregat A, Kotronoulas A, Marcos J, Joglar J, Alfonso I, Segura J, Ventura R, Pozo OJ.

Steroids, 78, 327-336, 2013

Chiral triazolium salts and ionic liquids: from the molecular design vectors to their physical properties through specific supramolecular interactions.

Porcar R, Ríos-Lombardía N, Busto E, Gotor-Fernández V, Montejo-Bernardo J, García-Granda S, Luis SV, Gotor V, Alfonso I, García-Verdugo E.

Chemistry. . Eur. J., 19, 892-904, 2013

The emergence of halophilic evolutionary patterns from a dynamic combinatorial library of macrocyclic pseudopeptides.

Atcher J, Moure A, Alfonso I.

Chem Commun 49, 487-489, 2013

Publications
(books and book chapters)

Chiral Molecular Receptors Based on Trans-Cyclohexane-1,2-Diamine.

Alfonso I.

Advances in Organic Synthesis, (Atta-ur-Rahman, Ed), Vol. 5, 51-100, 2013.

Receptors for Zwitterionic Species.

Luis SV, Alfonso I, Galindo F.

Supramolecular Chemistry: From Molecules to Nanomaterials. (Eds. Gale PA, Steed JW), John Wiley & Sons, Ltd., pp. 1259-1280, 2012

Research projects

Moléculas pseudopeptídicas: sistemas complejos de receptor-huésped, auto-ensamblaje y química constitucional dinámica

Nacional, CTQ2012-38543-C03-03

2013-2015

Aproximaciones no convencionales a la catálisis asimétrica: de nanomateriales inorgánicos a enzimas artificiales

Nacional, CTQ2012-38594-C02-02

2013-2015

Dynamic constitutional chemistry for the preparation of receptors for anions of biological interest

CCEE, 321659

2012-2016

Catálisis biomimética dirigida entrópicamente

Nacional, CTQ2011-14528-E

2011-2014

Emergence and Evolution of Complex Chemical Systems (SYSCHEM)

Unión Europea, Cost Action CM 1304
2013-2017

Prolonged inhibition of semaphorin3a pathway via a bio-degradable implant towards a better therapy for visual sensory impairments (VISION)

Unión Europea, C-HEALTH/1444

2012-2015

CHEMometric and High-Throughput Omics Analytical Methods for Assessment of Global Change Effects on Environmental and Biological Systems (CHEMAGEB)

Unión Europea, ERC-AdG 320327 (Romà Tauler, IDAEA)

2013-2017

Química combinatoria (covalente) dinámica aplicada a la preparación de receptores de aniones de interés biológico

Nacional, CTQ2009-14366-C02-02

2010-2012

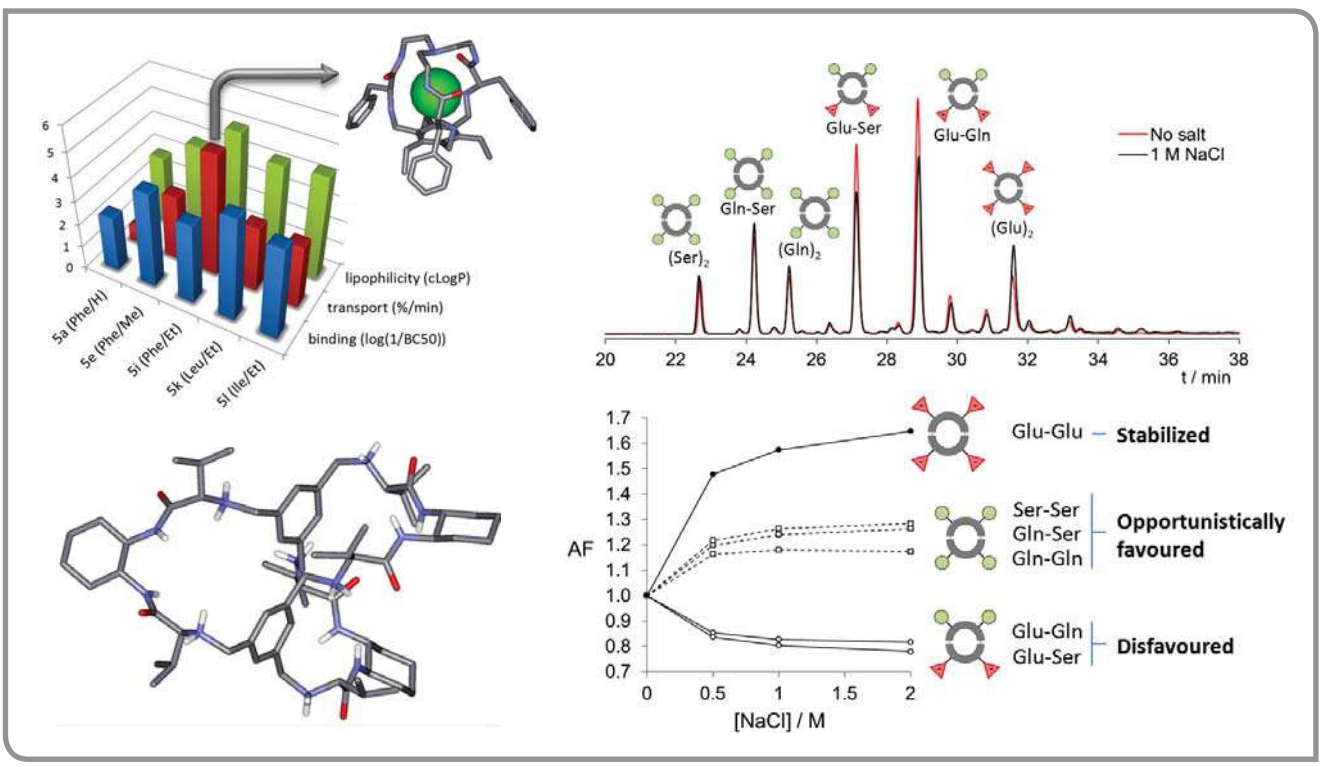
Catálisis biomimética dirigida entrópicamente (EnDeMiCat)

Ministerio de Ciencia e Innovación, CTQ2011-14528-E, acción complementaria Explora

2013-2014

Research Highlights

Following our work in Supramolecular Chemistry and Catalysis, we have obtained several remarkable results in the 2012-2013 period. The use of simple pseudo-peptidic cages for the binding of chloride anion has been reported.[1] We have characterized this interaction by different experimental techniques both in solution (ESI-MS and NMR) and in the solid state (X-ray diffraction). We observed that these simple synthetic cages were able to efficiently encapsulate the chloride ion, with different binding strength depending on the cage structure. Moreover, these small cages promoted the transport of chloride ion through lipid bilayers as models of cell membranes, with potential biological applications.[2] Other larger pseudopeptidic cages have been also prepared by a multicomponent [3+2] reductive amination reaction with pre-organized precursors. This pre-organization can be achieved by the suitable structural design of a rigid conformation of the precursors or upon the addition of an anionic template to the medium.[3]



On the other hand, we also advanced in the Systems Chemistry field with pseudopeptides. Using Nature as a source of inspiration, we designed a simple Dynamic Combinatorial Library of pseudopeptidic macrocycles, able to exchange through disulfide chemistry in aqueous solution containing a small amount of DMSO and at different pH values.[4] Very interestingly, these libraries behaved as simple model of chemical systems exerting evolutionary trends as a response of a meaningful and simple stimulus. Thus, the increase of the ionic strength induced the amplification of the members concentrating the acidic side chains (derived from aspartic or glutamic acids) that are anionic at the working pH.[5] This evolutionary process parallels with the one developed by the proteins of the halophilic organisms for retaining the functionality of their biomolecular machinery in highly saline media. Overall, this result highlights the importance of dynamic libraries within the new topic of Systems Chemistry.

(1) I. Martí, J. Rubio, M. Bolte, M.I. Burguete, C. Vicent, R. Quesada, I. Alfonso, S.V. Luis, *Chem. Eur. J.* **2012**, *18*, 16728-16741.

(2) I. Alfonso, R. Quesada, Chem. Sci. 2013, 4, 3009-3019.

(3) A. Moure, S.V. Luis, I. Alfonso, *Chem. Eur. J.* **2012**, *18*, 5496-5500.

(4) J. Atcher, I. Alfonso, *RSC Adv.* **2013**, *3*, 25605-25608.

(5) J. Atcher, A. Moure, I. Alfonso, *Chem. Commun.* **2013**, *49*, 487-489.

Ecological Chemistry

Our group deals with different aspects related with new insect pheromones, from structural characterization and synthesis of pheromones and analogues to determination of their attractant activity in the laboratory by electrophysiological techniques (electroantennogram and coupled gas chromatography-electroantennogram) and behavioral bioassays, as well as in the field. In addition, we are also involved in the development of new alternative, biorational and non-contaminant methods of pest control, based on inhibition of the enzymes responsible for the degradation of pheromone molecules at the insect's antennae..

STAFF

ANGEL GUERRERO PÉREZ, GROUP LEADER
Mª PILAR BOSCH VERDEROL
GLORIA ROSELL PELLISÉ

TECHNICIAN

JUANA Mª ROZALEN MECA

Ph. D.

CARMEN QUERO LÓPEZ
LOURDES MUÑOZ RUBIO
VICTORIA ELENA RAMOS MACIAS
SERGIO LOPEZ ROMERO

Ph. D. STUDENTS

BEN FURSTENAU
RAFAEL GAGO OTERO
MARC PUIGMARTI BORRELL

POST-GRADUATE STUDENTS

CARLOS SANCHEZ GARCIA
ANA ISABEL BERNABÉ MURCIA
BERTA VIDAL ALTEMIR

Publications (articles)

Mimicking insect communication: release and detection of pheromone, biosynthesized by an alcohol acetyl transferase immobilized in a microreactor.

Muñoz L, Dimov N, Carot-Sans G, Bula WP, Guerrero A, Gardeniers HJGE.

PLoS ONE 7(11), e47751, 2012

Moths behaving like butterflies. Evolutionary loss of long range attractant pheromones in Castniid moths: A Paysandisia archon model.

Monteys V, Acín P, Rosell G, Quero C, Jiménez MA, Guerrero A.

PLoS ONE 7(1), e29282, 2012

Electrophysiological and behavioral responses of the black-banded oak borer, Coroebus florentinus, to conspecific and host-plant volatiles.

Fürstenau B, Rosell G, Guerrero A, Quero, C.

J. Chem. Ecol. 38, 378–388, 2012

A carboxylesterase, Esterase-6, modulates sensory physiological and behavioural response dynamics to pheromone in Drosophila.

Chertemps T, François A, Durand N, Rosell G, Dekker T, Lucas P, Maïbèche-Coisné M.

Bmc Biology 10, 56-68, 2012

Synthesis of a new deuterium-labeled phytol as a tool for biosynthetic studies.

Muñoz L, Guerrero A.

Synthesis 44, 862–864, 2012

New identification of proanthocyanidins in cinnamon (Cinnamomum zeylanicum L.) using MALDI-TOF/TOF mass spectrometry.

Mateos-Martín ML, Fuguet E, Quero C, Pérez-Jiménez J, Torres JL.

Anal. Bioanal. Chem. 402, 1327–1336, 2012

Utilització de feromones d'insectes en un control integrat de plagues.

Guerrero A.

L'Atzavara 21, 57-67, 2012

Inhibition of the responses to sex pheromone of the fall armyworm, Spodoptera frugiperda.

Malo EA, Rojas JC, Gago R, Guerrero A.

J. Insect Sci. 13, 1-14, 2013, http://www.insectscience.org/13.134

A tetraene aldehyde as the major sex pheromone component of the promethea moth (Callosamia promethea (Drury)).

Gago R, Allyson JD, McElfresh JS, Haynes KF, McKenney J, Guerrero A, Millar J.

J. Chem. Ecol. 39, 1263–1272, 2013

Phytal: A Candidate Sex Pheromone Component of the Moroccan Locust Dociostaurus maroccanus.

Furstenau B, Muñoz L, Coca-Abia M, Rosell G, Guerrero A, Quero C.

ChemBioChem 14, 1450–1459, 2013

Electrophilic derivatives antagonise pheromone attraction in Cydia pomonella.

Sans A, Gago R, Mingot A, García W, Bosch D, Coll J, Rosell G, Bosch MP, Riba M, Guerrero A.

Pest Manag Sci 69, 1280–1290, 2013

Electrophysiological and behavioural responses of Pityophthorus pubescens (Coleoptera: Scolytinae) to (E,E)-α-farnesene, (R)-(+)-limonene and (S)-(–)--verbenone in Pinus radiata (Pinaceae) stands in northern Spain.

López S, Quero C, Iturrondobeitia JC, Guerrero A, Goldarazena A.

Pest Manag Sci. 69, 40-47, 2013

Publications
(books and book chapters)

Disrupción de la comunicación química de insectos como estrategia en un control biorracional de plagas.

Guerrero A, Sans A, Riba M.

Temas Selectos de Ecología Química (ed. J.C. Rojas, E.A. Malo), 427-446, ECOSUR (México), 2012.

Research Projects

Aproximación hacia un control de plagas de insectos de interés económico mediante disrupción de la comunicación química entre sexos

Nacional, AGL2012-39869-C02-01

2013-2015

Desarrollo de antagonistas de feromonas sexuales para un control biorracional de plagas de insectos. Actividad y estudios enzimáticos

Nacional, AGL2009-13452-C02-01

2010-2012

Ayudas para apoyar las actividades de los grupos de investigación para el año 2009. Nombre del grupo: Unitat d'Ecologia Quimica (UCE)

Generalitat de Catalunya, 2009SGR871

2009-2013

Obtención de atrayente para el control de moscas de la fruta de la especie Bactrocera oleae y de la especie Rhagoletis cerasi

SEDQ, S.A.

2013-2015

Subministrament d'atraients d'aplicació a trampes pel control de Coroebus undatus.

Generalitat de Catalunya, 2012

Research highlights

In this biennial period 2010-2011 the Chemical Ecology Group has accomplished the following main features:

1. Butterflies and moths show different reproductive behaviors. Whereas butterflies rely on visual stimuli for mate location, moths use the 'female calling plus male seduction' system, where females release long-range sex pheromones to attract conspecific males. There are few exceptions from this pattern but in all known cases female moths possess sex pheromone glands which apparently have been lost in female butterflies. This is the case in Castniidae ("butterfly-moths") in which no pheromone has been found so far. For the first time we present evidence that Paysandisia archon (Lepidoptera: Castniidae) females do not produce pheromone to attract males, and that mate location is achieved only visually by patrolling males, which release a pheromone at short distance, putatively a mixture of Z,E-farnesal, E,E-farnesal and (E,Z)-2,13-octadecadienol. These compounds were present in male wing extracts and display electrophysiological activity in female antennae (Figure 1). Farnesals have not been identified yet in palm trees, the only host plants known for P. archon. These plants contain E,E-farnesene and Z,E-farnesene, from which the corresponding alcohols could be biosynthesized and thus become precursors of the farnesals released by P. archon males.

Our results suggest a novel butterfly-like reproductive behavior in castniid moths (PLoS ONE 7, e29282, 2012). This will also have practical implications in applied entomology because it points out that the monitoring/control of castniid pests should not be based on the use of female-produced pheromones, as it is usual in many moths.

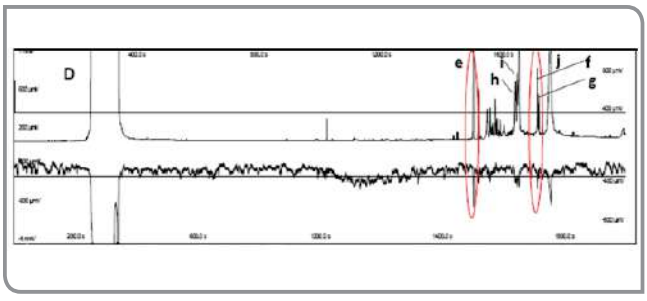


Figure 1. GC-EAD response of P. archon female antennae to a male wings extract. Compounds identification: a=nonanal, b=decanal, c=tetradecamethyl cycloheptasiloxane, d=hexadecamethyl cyclooctasiloxane, e=Z,E-farnesal, f=(E,Z)-2,13-octadecadienol, g=n-henicosane; h=(Z)-11-hexadecenoic acid; i=palmitic acid; j=oleic acid. Upper trace: FID response. Lower trace: EAD response. Red ellipses highlight Z,E-farnesal and (E,Z)-2,13-octadecadienol, two components of the putative male sex pheromone.

2. Infochemical production, release and detection of (Z,E)-9,11-tetradecadienyl acetate, the major component of the pheromone of the moth Spodoptera littoralis, is achieved in a novel microfluidic system designed to mimic the final step of the pheromone biosynthesis by immobilized recombinant alcohol acetyl transferase (PLoS ONE 7, e47751, 2012). The microfluidic system is part of an "artificial gland", i.e., a chemoemitter, which comprises a microreactor connected to a microevaporator and is able to produce and release a pre-defined amount of the major component of the pheromone from the corresponding alcohol. Performance of the entire chemoemitter has been assessed in electrophysiological and behavioral experiments. Electroantennographic depolarizations of the pheromone produced by the chemoemitter were ca. 40% relative to that evoked by the synthetic pheromone (Figure 2). In a wind tunnel, the pheromone released from the evaporator elicited on males a similar attraction behavior as 3 virgin females.

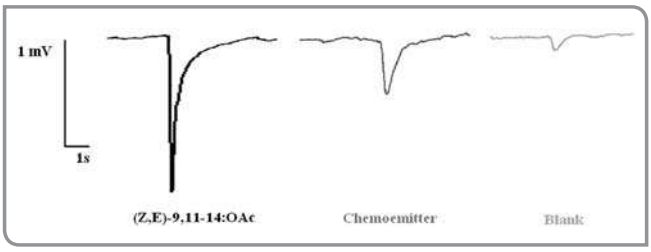


Figure 2. Electroantennographic detection of the pheromone (Z,E)-9,11-14:OAc, produced by two microreactors and emitted by the evaporator (chemoemitter, center) vs response to a filter paper containing 10 µg of the synthetic pheromone (left) and blank (right).

3. Studies designed to investigate the chemical ecology of the black-banded oak borer Coroebus florentinus (Coleoptera: Buprestidae) have been performed for the first time. Nonanal, decanal, and geranylacetone were identified in the headspace volatiles of both sexes, and found active on male antennae but scarcely on females. In dual-choice olfactometer experiments, blend of these compounds was attractive to both sexes, with males responding particularly to decanal alone and females to geranylacetone suggesting that these two compounds are responsible for activity of the blend to the respective sexes. Antennae of both sexes responded electroantennographically to the green leaf volatiles (GLVs) (E)-2-hexenal, (E)-2-hexenol, 1-hexanol, (Z)-3-hexenyl acetate, and n-hexyl acetate, all identified from the host plant Quercus suber. In behavioral experiments, only females were attracted to host-plant odors, particularly to (E)-2-hexenol, 1-hexanol, and (Z)-3-hexenyl acetate (Figure 3), suggesting that these compounds could play an important role in the foraging and/or oviposition behavior of C. florentinus females (J. Chem. Ecol. 38, 378, 2012).

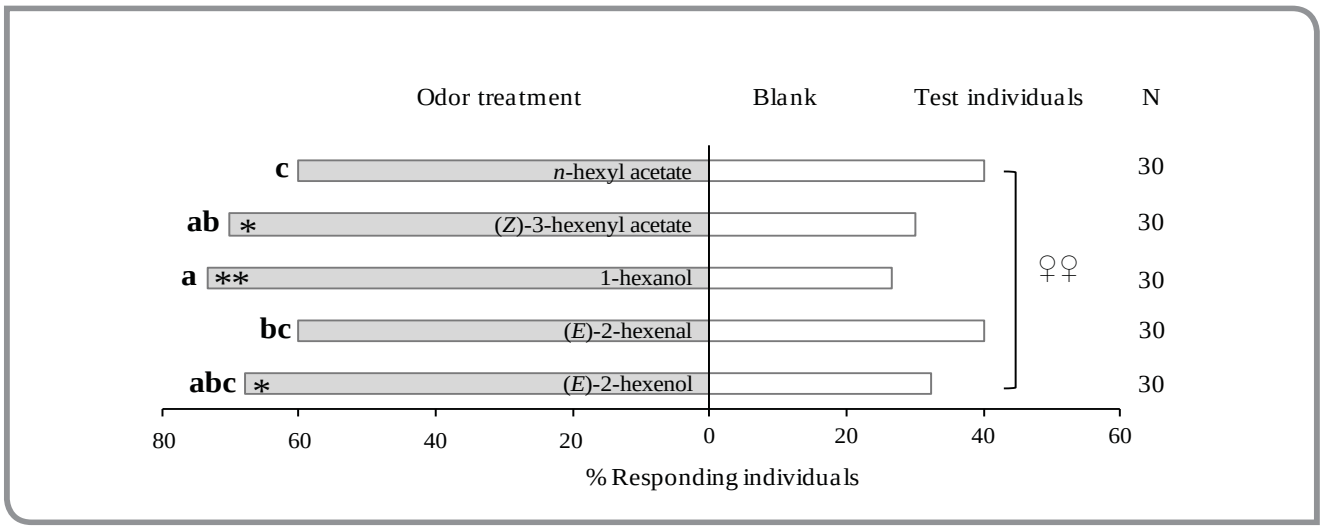
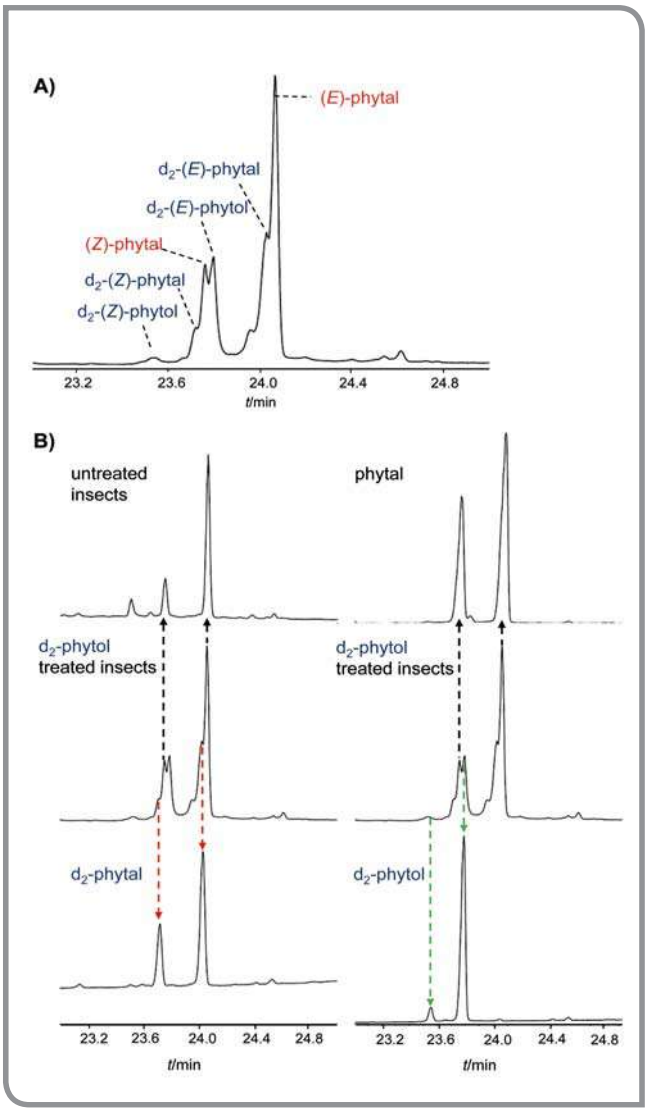


Figure 3. Behavioral responses of C. florentinus virgin females in a Y-tube olfactometer to the synthetic GLVs (E)-2-hexenal, (E)-2-hexenol, 1-hexanol, (Z)-3-hexenyl acetate and n-hexyl acetate. Number of insects attracted to odors were analyzed by χ2 goodness-of-fit test with Yates correction for continuity (*P≤0.05; **P≤0.01). Bars with different letters indicate significant differences between ratios (test/control) of the treatments (one-way ANOVA followed by Tukey's HSD test; P≤0.05). N = number of responding individuals.

Figure 4. A) Partial GC profile of an adult male leg extract showing compounds identified after treatment with d_2-phytol. B) Partial GC profile of a leg extract of the Moroccan locust adult males after treatment with d_2-phytol (middle) in comparison to untreated insects (upper left) and synthetic d_2-phytal (bottom, left), and with synthetic (Z/E)-phytal (upper right) and d_2-phytol (bottom right). Peaks of identified compounds are marked by coloured arrows (black = phytal; red = d_2-phytal; green = d_2-phytol).

4. For the first time, we have carried out studies directed to control the Moroccan locust, Dociostaurus maroccanus, a polyphagous pest of crops particularly in Southern Europe, North Africa and the Middle East, and we have found that both isomers of phytal (3,7,11,15-tetramethyl-2-hexadecenal) are involved in the chemical communication and behaviour of the pest (ChemBioChem 14, 1450, 2013). This compound was identified by comparison of its chromatographic and spectrometric features and microchemical reactions with those of a synthetic sample. The natural compound has the R,R configuration by chiral HPLC analysis and its structure is unique as an insect pheromone component. Both isomers of phytal are produced by sexually mature adult males and elicit electroantennographic responses on antennae of both sexes. In two-choice olfactometer bioassays, males and females significantly preferred the stream enriched with racemic phytal to control. Both isomers of phytal are specific to D. maroccanus as they are absent in the closely related, habitat-sharing species Dociostaurus jagoi and Calliptamus wattenwylianus. Legs and wings are the main release sites of the compound producing ca. 90% of the amount emitted by living individuals. In biosynthetic studies, phytal appears to proceed from oxidation of phytol, after injection of deuterated phytol (Synthesis 44, 862, 2012) into the abdomen of the insect or after administration on the diet (Figure 4). Our results point out that phytal is a candidate sex pheromone component of the Moroccan locust produced by mature males, which may be eavesdropped by conspecific males.



5. We have prepared and tested new non-fluorinated electrophilic derivatives structurally related to the pheromone of Cydia pomonella (codlemone) as putative pheromone antagonists, and therefore as disruptants of the pheromone communication of the insect. We synthesized codlemone (1) in excellent stereoselectivity in a new, iterative approach involving two Horner-Wadsworth-Emmons reactions. The new antagonists, (E,E)-(10,12)-tetradecadien-2-one (2), methyl (E,E)-(10,12)-2-oxo-tetradecadienoate (3), and (E,E)-(11,13)-pentadecadien-2,3-dione (4), were obtained from codlemone in straightforward approaches in good overall yields and excellent stereochemical purity (≥98% E,E). In electrophysiology, only compound 2 displayed inhibition of the antennal response to the pheromone after presaturation of the antennal receptors.

Although compounds 2-4 did not inhibit the pheromone degrading enzyme responsible for codlemone metabolism, mixtures of ketone 2 and diketone 4 with codlemone elicited erratic flights on males in a wind tunnel. In the field, blends of compound 2 or 4 with the pheromone in 10:1 ratio caught significantly fewer males than codlemone alone (Figure 5). Our results suggest that it may be worthwhile conducting new, larger-scale studies on the activity of methyl ketones as disruptants of pheromone communication to evaluate the real prospects of compounds of this type as potential control agents.

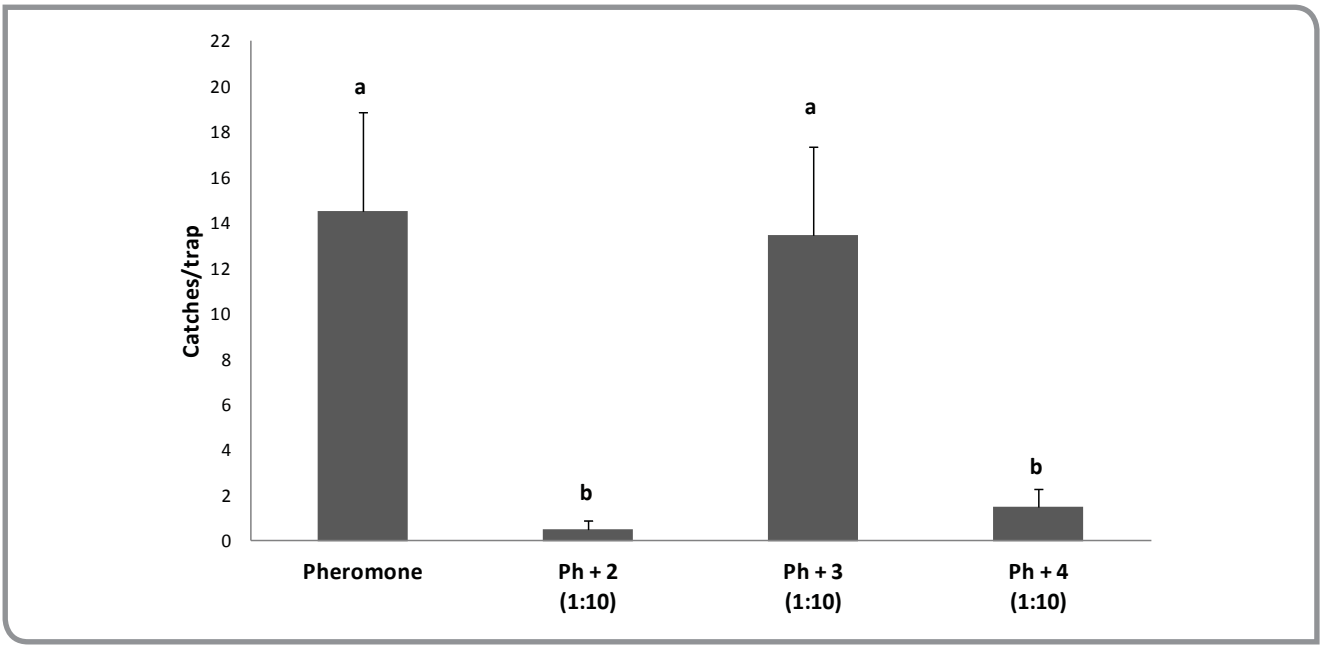


Figure 5. Mean (±SD) number of catches of C. pomonella males per trap baited with codlemone (pheromone), mixtures of codlemone and methyl ketone 2, codlemone and keto ester 3 and codlemone and diketone 4 in 1:10 ratio. Bars with the same letter are not significantly different (Duncan's test, $P < 0.05$).

Theoretical and Computational Chemistry

The Theoretical and Computational Chemistry Group (QTC) studies the structure and reactivity of molecules using the computational methods of Theoretical Chemistry. Special interest is devoted to two main areas:

- Oxidation reactions playing an important role in atmospheric and environmental chemistry, as well as in biological systems
- Protein dynamics, with special interest in enzyme catalysis, thermostability, and Intrinsically Disordered Proteins.

STAFF

JOSEP M. ANGLADA RULL , GROUP LEADER
SANTIAGO OLIVELLA NELLO
RAMON CREHUET SIMON

Ph. D.

MIQUEL TORRENT-SUCARRAT

Ph. D. STUDENTS

ENRIQUE MARCOS BENTEO
MELCHOR SANCHEZ MARTINEZ

Publications (articles)

Sulfuric acid as autocatalyst in the formation of sulfuric acid.

Torrent-Sucarrat M, Francisco JS, Anglada JM

J. Am. Chem. Soc., 134, 20632-20644, 2012

Theoretical study of the switching between Hückel and Möbius topologies for expanded porphyrins.

Marcos E, Anglada JM, Torrent-Sucarrat, M.

J. Phys. Chem. C, 116, 24358-24366, 2012

Is the HO_4^- anion a key species in the aqueous-phase decomposition of ozone?.

Anglada JM, Torrent-Sucarrat M, Ruiz-Lopez MF, Martins-Costa M.

Chem. Eur. J., 18, 13435 – 13445, 2012

Correlation between photophysical parameters and gold–gold distances in Gold(I) (4-pyridyl) ethynyl complexes.

Rodríguez L, Ferrer M, Crehuet R, Anglada J, Lima JC.

Inorg. Chem., 51, 7636–7641, 2012

Reactivity of volatile organic compounds at the surface of a water droplet.

Martins-Costa MTC, Anglada JM, Francisco JS, Ruiz-Lopez MF.

J. Am. Chem. Soc., 134, 11821–11827, 2012

Effects of a single water molecule on the OH + H_2O_2 reaction.

Buszek, RJ, Torrent-Sucarrat M, Anglada JM, Francisco JS.

J. Phys. Chem. A, 116, 5821–5829, 2012

Reactivity of atmospherically relevant small radicals at the air-water interface.

Martins-Costa MTC, Anglada JM, Francisco JS, Ruiz-Lopez MF.

Angew. Chem. Int. Ed., 124(22), 5413-7, 2012

Evaluation of the nonlinear optical properties for an expanded porphyrin Hückel-Möbius aromaticity switch.

Torrent-Sucarrat M, Josep Anglada JM, Luis J.

J. Chem. Phys., 137, 184306, 2012

Dynamic fingerprints of protein thermostability revealed by long molecular dynamics.

Marcos E, Aurora Jiménez A, Crehuet R.

J. Chem. Theory Comput., 8, 1129–1142, 2012

Conformational compression and barrier height heterogeneity in the N-acetylglutamate kinase.

Sanchez-Martinez M, Marcos E, Tauler R, Field MJ, Crehuet R.

J. Phys. Chem. B, 117(46), 14261–14272, 2013

The reaction of formaldehyde carbonyl oxide with the methyl peroxy radical and its relevance in the chemistry of the atmosphere.

Anglada JM, Olivella S, Solé A.

Phys. Chem. Chem. Phys., 15, 18921-18933, 2013

Atmospheric significance of water clusters and ozone–water complexes.

Anglada JM, Hoffman GJ, Slipchenko LV, Costa M, Ruiz-López MF Francisco JS.

J. Phys. Chem. A, 117(40), 10381–10396, 2013

SS-map: Visualizing cooperative secondary structure elements in protein ensembles.

Iglesias J, Melchor Sanchez-Martinez M, Crehuet R.

Intrinsically Disordered Proteins 1, e25323; 2013

The gas-phase reaction of methane sulfonic acid with the hydroxyl radical without and with water vapor.

Jørgensen S, Jensen C, Kjaergaard HG, Anglada JM.

Phys. Chem. Chem. Phys., 15, 5140-5150, 2013

Research projects

Descripción de proteínas intrínsecamente desordenadas mediante la integración de datos de RMN y SAXS a simulaciones coarse grained

Nacional, CTQ2012-33324

2013-2015

Estudio teórico de reacciones de oxidación iniciadas por HO, O3 y NO3

Nacional, CTQ2011-27812

2010-2014

Acoplamiento entre dinámica y catálisis en los enzimas. Desarrollo de métodos y estudio de la familia de la kinasa de NAG y de las aldolasas de clase II

Nacional, CTQ2009-08223

2010-2012

Möbius aromaticity: a new challenge for computational chemistry.

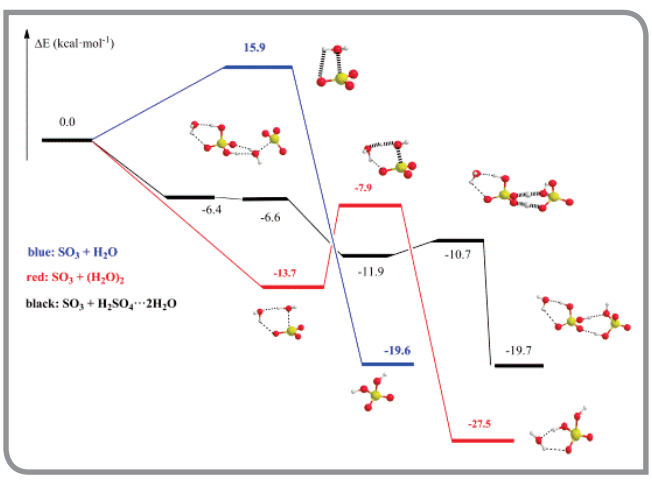
CCEE, 249310

2009-2012

Research highlights

Sulfuric acid can catalyze its own formation:

Sulfuric acid is an important species in the Earth's atmosphere.It contributes to acid rain and to atmospheric nucleation processes and therefore it has a great impact on environment, on human health and



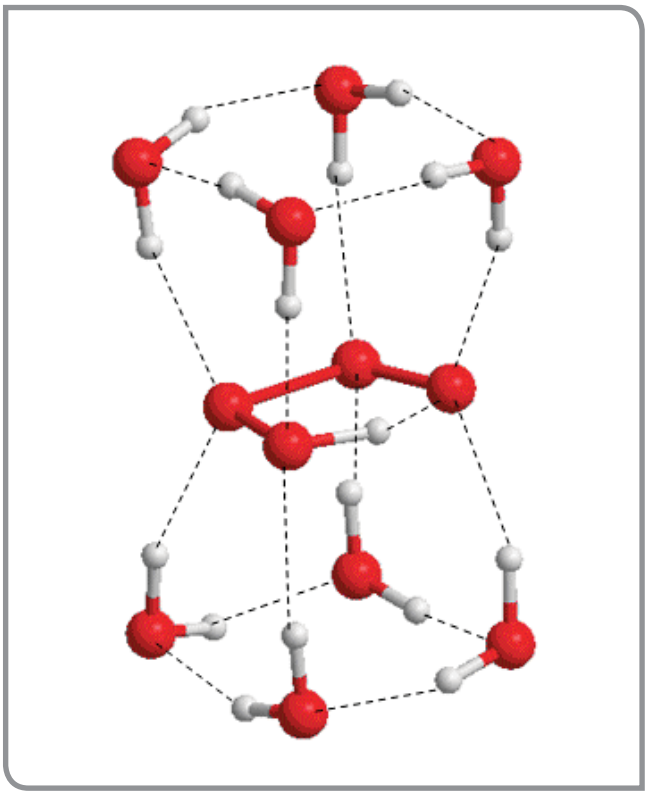
in climate change. The well known mechanism for the atmospheric formation of H_2SO_4 involves the hydrolysis of SO_3 requiring the simultaneous participation of two water molecules. Our results predict that one molecule of sulfuric acid can replace one of the water molecules producing an important catalytic effect. These results have broad implications in the heterogeneous formation of sulfuric acid, in the atmospheric formation of aerosols, in the H_2SO_4 formation of aircraft engines and also in the understanding of formation of sulfuric acid in the atmosphere of Venus. J. Am. Chem. Soc., 2012, 134, 20632.

Chemistry at the air-water interface:

The knowledge of the chemistry at the air-water interface is relevant because its importance on atmospheric issues regarding aerosols and water droplets. Several investigations have provided evidence that chemistry in aerosols and droplets often occurs at the surface and this is still poorly understood. In our research we have investigated, employing QM/MM (Quantum Mechanics/Molecular Mechanics) methods, the behavior of formaldehyde, the hydroperoxide radical and the superoxide anion in the air-water interface. Our results show that electronic interactions at the water surface can influence the chemical reactivity to a large extent than in bulk, and indicate that the surface of water droplets may play a significant role in the chemistry of the atmosphere. J. Am. Chem. Soc., 2012, 134, 11821-11827; Angew. Chem., 2012, 124, 5509-5513.

The HO_4^- anion in the aqueous-phase decomposition of ozone.

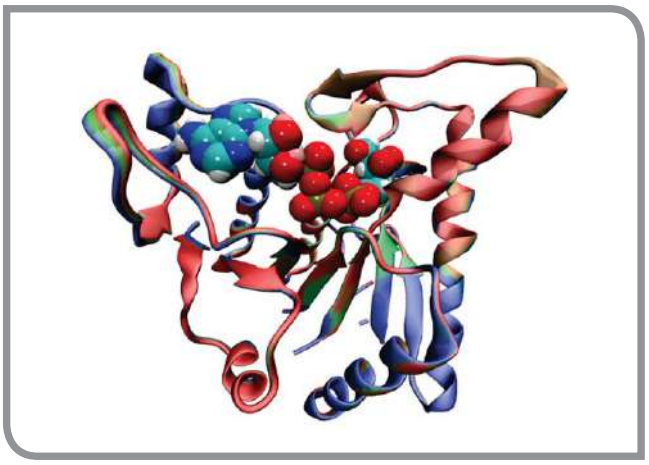
Ozone is unstable in water and its decomposition produces the highly reactive hydroxyl radical. Despite the whole mechanism is not well understood, it is assumed that ozone decomposition begins with reaction with the HO^- anion and follows a series of reaction involving electron transfer processes or the HO_3 radical intermediate. Addition of H_2O_2/HO_2^- also favors the process, which is known as peroxone chemistry. It has been also suggested that the HO_4^- adduct should play an important role in the series of reactions involving ozone decomposition in water. We have performed large scale ab-initio and QM/MM calculations regarding the thermochemistry of the main reactions contributing to ozone decomposition in water and the electronic and dynamical features of the HO_4^- adduct, and our results predict that its concentration would be smaller than reported previously. Chem. Eur. J., 2012, 125, 13435-13445.



Conformational Compression affects enzyme catalysis

The role of protein dynamics on enzyme catalysis is still an open question. In this work we performed hybrid QM/MM calculations on a kinase characterized by Rubio and colleagues. This kinase has two lids that open to let substrates in and out, but that, when closed, contribute to the catalytic effect by correctly positioning the substrates. We showed that the local conformation of the enzyme determines the energy barrier for the catalysis. Conformations where reactants are closer to each other and with a linear angle of attack have a lower barriers. These barriers are so low that the limiting step seems to be determined by protein conformational motions.

M Sanchez-Martinez, E Marcos, R Tauler, M Field, R Crehuet. J. Phys. Chem. B, 2013, 117, 14261-14272.

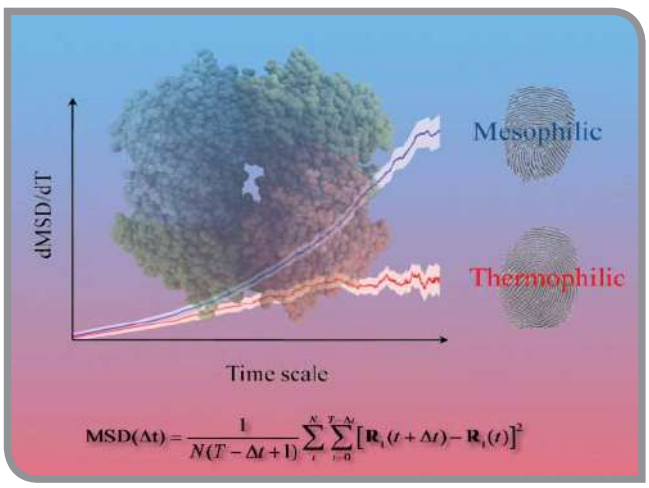


Hotter but not stiffer

If proteins of organisms that live at normal temperatures (mesophiles) denature at high temperatures, how do proteins stable at high temperature (belonging to thermophiles) behave?

We studied a thermophilic-mesofilic pair of proteins at different temperatures with Molecular Dynamics. Our results show that, the thermophilic protein is not more rigid at low temperatures as it was usually suspected. The crux of the difference is that the thermophilic protein retains its flexibility at high temperature whereas the mesophilic protein increases its flexibility with temperature at a high degree. Eventually this leads to its denaturation. Molecular Dynamics show that ion pairs contribute substantially to this different behaviour.

E Marcos, A Jiménez, R Crehuet. J. Chem. Theory and Comput., 2012, 8, 1129-1142.



Bioorganic Chemistry Group

We use the modern medicinal chemistry techniques (combinatorial chemistry, in silico design and construction of chemical libraries, solid phase synthesis, drug delivery methods) for the identification of hit compounds against targets of pharmacological interest. Complementarily, the chemical modulation of these hits for their conversion into lead compounds for further development in collaboration with pharma and biotech companies is intensively pursued.

STAFF

ANGEL MESSEGUER PEYPOCH, GROUP LEADER
FRANCISCA REIG ISART

Ph. D.

ASUNCION BURGUETE PEREZ
ESTHER CARRASCO ROMERO
NATALIA DE LA FIGUERA
MIRIAM CORREDOR
FEDERICO RUA
ANA VÁZQUEZ
MARÍA GARRIDO

TECHNICIANS

CRISTIAN LASTRE

Ph. D. STUDENTS

LAURA VAZQUEZ
MIQUEL VIDAL MOSQUERA

Publications (articles)

Synthesis of enantiomerically pure perhydro-1,4-diazepine-2,5-dione and 1,4-piperazine-2,5-dione derivatives exhibiting potent activity as apoptosis inhibitors.

Moure A, Orzáez M, Sancho M, Messeguer A.

Bioorg. Med. Chem. Lett., 22, 7097-7099, 2012

Advances in modulating thermosensory TRP channels.

Ferrer-Montiel, A.; Fernández-Carvajal, A.; Planells-Cases, R.; Fernández-Ballester, G.; González-Ros, J.M.; Messeguer, À.; González-Muñiz, R.

Expert Opin Ther Pat., 22(9), 999-1017, 2012.

Interfacial behavior of chroman-6 and chroman-6 palmitoyl ester and their interaction with phospholipids.

García-Antón JM, Reig F, Messeguer A, Comelles F, Espina M, Alsina MA,

Colloid Polym Sci, 291, 1065–1075, 2013 .

15N NMR spectroscopic and theoretical GIAO-DFT studies for the unambiguous characterization of disubstituted 1,2,3-triazoles.

Corredor M, Bujons J, Messeguer À, Alfonso I.

Org Biomol Chem.,11(42), 7318-7325, 2013.

Vestibulotoxic properties of potential metabolites of allylnitrile.

Rúa F, Buffard M, Sedó-Cabezón L, Hernández-Mir G, de la Torre A, Saldaña-Ruíz S, Chabbert C, Bayona JM, Messeguer A, Llorens

J. Toxicol Sci., 135(1),182-92, 2013.

Optimizing the control of apoptosis by amide/triazole isosteric substitution in a constrained peptoid.

Corredor M, Bujons J, Orzáez M, Sancho M, Pérez-Payá E, Alfonso I, Messeguer A.

Eur J Med Chem., 63, 892-896, 2013.

BH3-mimetics- and cisplatin-induced cell death proceeds through different pathways depending on the availability of death-related cellular components.

Andreu-Fernández V, Genovés A, Messeguer A, Orzáez M, Sancho M, Pérez-Payá E.

PLoS One, 8(2), e56881, 2013.

A polymeric nanomedicine diminishes inflammatory events in renal tubular cells.

Ucero AC, Berzal S, Ocaña-Salceda C, Sancho M, Orzáez M, Messeguer A, Ruiz-Ortega M, Egido J, Vicent MJ, Ortiz A, Ramos AM.

PLoS One, 8(1):e51992, 2013.

Research Projects

Prolonged inhibition of semaphorin3a pathway via a bio-degradable implant towards a better therapy for visual sensory impairments

CCEE, 304884

2012-2015

Modulación química de rutas de señalización celular relevantes en enfermedades degenerativas: generación de cabezas de serie

Nacional, SAF2011-30542-C02-01

2012-2014

Desarrollo de nuevas moléculas con actividad agonista del factor de crecimiento nervioso.

2011-2012

Estudios de formación de radicales libres en piel y protección o inhibición del proceso mediante aditivos antiradicalarios.

2011-2012

Diseño y síntesis de análogos químicos de inhibidores de quinasas descubiertos por Allinky.

Allinky Biopharma, S.A.

2009-2015

Consolider ingenio 2010: equipo de investigacion "the Spanish ion channel initative (sici) para investigación.

2008-2014

Bionure Farma, S.L.

Research Highlights

Our group became interested in this field in 1998. Through the establishment of collaborative projects with different laboratories, the group has been pioneer in Spain in the design and construction of combinatorial libraries of organic molecules, in particular of libraries of controlled mixtures of small organic molecules. In this period, libraries of peptoid mixtures (5.000 and 11.000 N-alkylglycine trimers, and 625 pentamers, respectively) and four libraries of individual components (peptidomimetics bearing heterocyclic moieties) have been prepared. In addition, libraries of peptidomimetics attached to microplates (Chem Chips) have been also constructed.

Along this period, our group has incorporated the required expertise for handling the different methodologies to work on Combichem (solid-phase organic synthesis, synthesis of libraries in solution, libraries of individuals or mixtures, use of microwave activation of organic reactions, in silico methodology for the design and screening of virtual libraries etc.). By using this general strategy, our group has obtained highly interesting results. Thus, we identified two peptoids that exhibit high in vitro and in vivo activity as blockers of the TRPV1 vanilloid receptor. In addition, and also in collaboration with the same partners, a family of molecules exhibiting potent antagonist activity against the NMDA receptor was identified. Moreover, the identification of a peptoid capable of inhibiting Sema-3 and thus interesting for studying the axonal regeneration problem, has been recently achieved

More recently, in collaboration with the group of Dr. E. Pérez-Payá (CIPF, Valencia), two compounds that neutralise bacterial endotoxins have been identified. In a parallel study in collaboration with the same group, peptoids capable of inhibiting the formation of apoptosome have been discovered. These compounds have been intellectually protected and the patent has been licensed to a pharmaceutical company for co-development. This result represents the first example of a small molecule as inhibitor of apoptosis operating by this mechanism and it also constitutes an interesting example of how small molecules can perturb and even modulate protein-protein interactions. A further con-

version of the initial hit into a peptidomimetic exhibiting improved activities in vitro and in vivo has been also carried out. The co-development of this compound in the organ transplant field is currently under contracted research with the above pharmaceutical company.

In a collaboration established with the group of Dr. Timothy Thomson (IMBM-CSIC, Barcelona), we have also identified peptoids capable of perturbing protein-protein interactions (UBC13-UEV) of interest in cancer and inflammation. What is interesting of this example and of some other commented above (for instance, the inhibitor of apoptosome), is that we have done already a step ahead in order to convert the identified hits into compounds exhibiting more friendly pharmacological profiles. Our goal is the selection of a lead candidate.

This structural conversion has been carried out by an initial study of the conformational preferences of the peptoid skeleton followed by the design of conformationally restricted analogues bearing different types of heterocyclic scaffolds. At this moment, we have one peptidomimetic showing high inhibitory activity of the apoptosome in intact cells. Moreover, a new generation of apoptosis inhibitors bearing a novel heterocyclic skeleton, already patented, has been also developed. Likewise, two peptidomimetics have been prepared following a molecular modelling study for improving the properties of the initial hit discovered in the above commented modulation of UBC13-UEV interaction. It should be remarked that this discovery represents the development of the first modulators of this protein-protein interaction that can show a highly promising activity in cancer treatment.

Our work on compounds that exhibit bioactive activity has been complemented by research on free radicals quenchers, either from oxygen (ROS) and/or nitrogen (RNS). Some years ago we discovered a tocopherol surrogate (CR-6) bearing a simple structure and potent activity as lipid peroxidation inhibitor. More recently, its activity as inhibitor of RNS species (NO and peroxynitrite) was also shown. Our laboratory participated with a biotech company, the Lipotec Group, in the industrial development of this antioxidant. This compound is now in Phase II clinical trials in antitumour therapy, specifically in preparations containing liposomes that encapsulate doxorubicin. CR-6 is embedded in these liposomes and reduces the side-effects produced by the anticancer drug. Moreover, CR-6 is being commercially used in the dermopharmacy area as antiageing agent. On the other hand, recent work has shown the ability of CR-6 to inhibit apoptosis in photoreceptor cells (collaboration with T. Cotter, Univ. of Cork, Ireland). Likewise, in the frame of a collaboration established with the group of A. Planas (IIBB-CSIC, Barcelona), very interesting results on the potential neuroprotective activity of CR-6 have been obtained.

Taken together, all these results show the high therapeutic potential of this radical inhibitor. Currently, we have designed and synthesised a collection of CR-6 analogues capable of eliciting a higher penetration through the blood brain barrier. The results obtained up to date have identified 3 compounds exhibiting a satisfactory penetrability through different models of this barrier. Complementarily, these hit compounds will be assayed as anticancer agents and their potential conjugation to molecules that have properties as selected Alzheimer targets will be explored.

Finally, it is worth of mentioning the intense activity of our group in three additional fields. First, we are members of a Consolider Consortium focused on Ion Channels and financed up to 2013 and extended through 2013. This Consortium is coordinated bycoordinated by Prof. Antonio Ferrer-Montiel (Univ. Miguel Hernández). Our main task is to provide with molecules (libraries or individuals) to more than 20 research groups working on ion channels and interested in the identification of compounds that can modulate the function of these channels. On the other hand, our group is working intensively in two research projects supported by private pharma or biotech companies. In both cases it is intended to discover lead compounds active in front of highly interesting pharmaceutical targets.

Finally, as consequence of a publication from 2009 where in collaboration with Prof. Eduardo Soriano (University of Barcelona) we reported the identification of SICHI, a peptoid capable of inhibiting Semaphorin 3A, we were invited to participate in a European Project together with three companies from Israel, Germany and Spain, and a research group from the University of Tel-Aviv. This Project, called VISION, has been granted and it is currently in due course.

Biologically Active Phytochemicals

The BAP research group has a long-standing interest in the structural elucidation of new natural compounds of plant origin (sesquiterpenoids related to insect juvenile hormones and the associated chromene antagonists precocenes; diterpenes as insect anti-feedants; insect molting hormone agonist or antagonist steroids or ecdysteroids) and their biological activities. Other research has involved rotenoids, furanocoumarins, iridoid glycosides, anthraquinones, bibenzyls, sterols,… Nowadays, the main goals are the prospective development of new eco-friendly and sustainable insect pest-control agents from plants and to provide basic knowledge for new applications, safety and quality-control reasons of other aromatic and medicinal plants components.

STAFF

JOSEP COLL TOLEDANO
TECHNICIAN
JOAN LLORIA TOLRÀ

Publications (articles)

Preparation and characterization of persistent maltose-conjugated triphenylmethyl radicals.

Mesa JA, Velázquez-Palenzuela A, Brillas E, Coll J, Torres JL, Juliá L.

J. Org. Chem. 77, 1081-1086, 2012

A cell-based reporter assay for screening for EcR agonist/antagonist activity of natural ecdysteroids in Lepidoptera (Bm5) and Diptera (S2) cell cultures, followed by modeling of ecdysteroid-EcR interactions and normal mode analysis.

Zotti MJ, Geyter E, Swevers L, Braz A.S.K., Scott LPB, Rougé P, Coll J, Grutzmacher AD, Lenardão EJ, Smagghe G.

Pesticide Biochem. Physiol. 107, 309–320, 2013

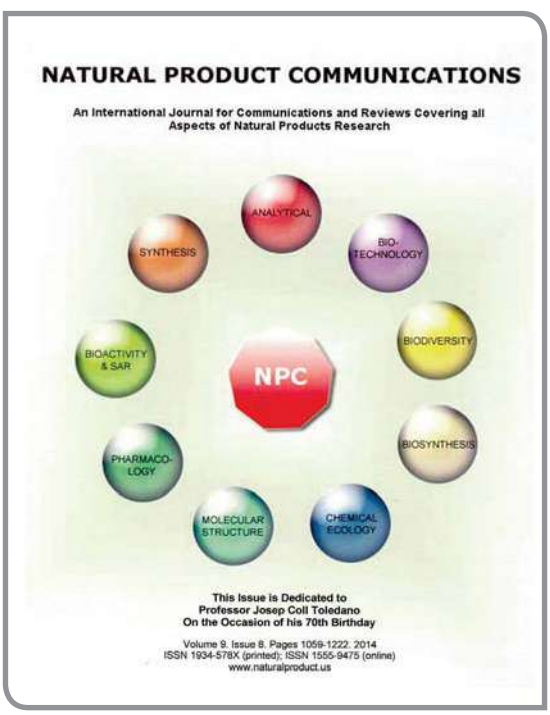
Electrophilic derivatives antagonise pheromone attraction in Cydia pomonella.

Sans A, Gago R, Mingot A, García W, Bosch D, Coll J, Rosell G, Bosch MP, Riba M, Guerrero A.

Pest Manag. Sci. 69, 1280–1290, 2013

Highlights

Special issue dedicated to Dr. Coll



Department of Biomedicinal Chemistry

Department of Biomedicinal Chemistry

Head: Gemma Fabriàs Domingo / Amadeu Llebaria Soldevila

The Department of Biomedicinal Chemistry conducts multidisciplinary research focused on the biomedical applications of peptides, lipids and glycoconjugates. The early detection, markers discovery and treatment of serious human diseases, such as amyloidosis related to the protein transthyretin, chronic pain, sphingolipidosis, cancer, neurodegeneration, autoimmune and infectious diseases, are emphasized. The investigations encompass the rational design of active molecules (peptides, glycoconjugates and small molecular entities) based on the knowledge of specific cell signalling routes, metabolic pathways, mechanisms of ligand-protein interactions, etc., as well as the concept of chemical modulation for optimising hit compounds based upon the modern medicinal chemistry technologies (combinatorial chemistry, in silico design and screening, solid phase organic synthesis, delivery systems).

Research groups

- Research Unit on BioActive Molecules
- Synthesis and Biomedical Applications of Peptides
- Unit of Glycoconjugate Chemistry
- Chemical Biology
- Medicinal Chemistry

Research Unit on BioActive Molecules

The Research Unit on BioActive Molecules works on the discovery of small molecules with activity on biologically relevant processes, with special interest on sphingolipid metabolism and functions. Sphingolipids play essential roles in the outcome and progression of diseases, including both rare diseases (sphingolipidosis) and diseases of high socio-economic impact (cancer, infectious diseases, diabetes 2, neurodegenerative diseases, etc.) thereby providing attractive targets to develop tools of use in diagnosis and prognosis, and leads in drug discovery. The research conducted encompasses from the design and synthesis of molecules and libraries to their biological study in cell lines, including sphingolipidomics.

STAFF

GEMMA FABRIAS DOMINGO, GROUP LEADER
JOSE LUIS ABAD SAIZ
JOSEFINA CASAS BRUGULAT
ANTONIO DELGADO CIRILO

TECHNICIANS

PEDRO RAYO PIZARROSO

Ph. D.

CARMEN BEDIA GIRBÉS

Ph. D. STUDENTS

FRANCESCA CINGOLANI
INGRID NIEVES CALATRAVA
YADIRA ORDÓÑEZ VIVANCO
MIREIA CASASAMPERE
POL SANLLEHÍ FIGUEROLA
ANA PAU CABELLO
RAQUEL CALDERON ALMENDRO

Publications (articles)

Dihydroceramide delays cell cycle G1/S transition via activation of ER stress and induction of autophagy.

V Gagliostro, J Casas, A Caretti, JL Abad, L Tagliavacca, R Ghidoni, G Fabrias, P Signorelli.

Int J Biochem Cell Biol, 44, 2135– 2143, 2012

Cellular changes that accompany shedding of human corneocytes.

Lin, T. K.; Crumrine, D.; Ackerman, L. D.; Santiago, J. L.; Roelandt, T.; Uchida, Y.; Hupe, M.; Fabrias, G.; Abad, J. L.; Rice, R. H.; Elias, P. M.,

J. Invest. Dermat., 132, 2430-2439, 2012

Identification of phototransformation products of sildenafil (Viagra) and its N-demethylated human metabolite under simulated sunlight.

Eichhorn P, Pérez S, Aceña J, Gardinali P, Abad JL, Barceló D.

J. Mass. Spectrom., 47, 701–711, 2012

Accumulated bending energy elicits neutral sphingomyelinase activity in human red blood cells.

López DJ, Egido-Gabas M, López-Montero I, Busto JV, Casas J, Garnier M, Monroy F, Larijani B, Goñi FM, Alonso A.

Biophys. J., 102, 2077-85, 2012.

Sialyllactose in Viral Membrane Gangliosides Is a Novel Molecular Recognition Pattern for Mature Dendritic Cell Capture of HIV-1.

Izquierdo-Useros N, Lorizate M, Contreras FX, Rodriguez-Plata MT, Glass B, Erkizia I, Prado JG, Casas J, Fabriàs G, Kräusslich H-G, Martinez-Picado J.

PLoS Biol 10(4), e1001315, 2012

In situ synthesis of fluorescent membrane lipids (ceramides) using click chemistry. Garrido M, Abad JL, Alonso A, Goñi FM, Delgado A, Montes LR.

J. Chem. Biol., 5, 119-123, 2012

3-Deoxy-3,4-dehydro analogs of XM462. Preparation and activity on sphingolipid Metabolism and Cell Fate.

Camacho L, Simbari F, Garrido M, Abad JL, Casas J, Delgado A, Fabriàs G.

Bioorg. Med. Chem., 20, 3173-3179, 2012

Fenretinide prevents lipid-induced insulin resistance by blocking ceramide biosynthesis.

Bikman BT, Guan Y, Shui G, Siddique MM, Holland WL, Kim JY, Fabriàs G, Wenk MR, Summers SA.

J. Biol. Chem., 287, 17426-17437, 2012

Sphingosine mediates TNF–alpha induced lysosomal membrane permeabilization and ensuing programmed cell death in hepatoma cells.

Ullio C, Casas J, Brunk UT, Sala G, Fabrias G, Ghidoni R, Bonelli G, Baccino FM, Autelli R.

J. Lipid. Res., 56, 1134-1143, 2012

Determination of sphingosine-1-phosphate lyase activity by gas chromatography coupled to electron impact mass spectrometry.

Reina E, Camacho L, Casas J, Van Veldhoven PP, Fabriàs G.

Chem Phys Lipids, 165(2), 225-231, 2012

Dihydroceramide desaturase and dihydrosphingolipids: Debutant players in the sphingolipid arena.

Fabriàs G, Munoz-Olaya J, Cingolani F, Signorelli P, Casas J, Gagliostro V, Ghidoni R.

Prog Lipid Res 51, 82–94, 2012

Generation of a human neuronal stable cell model for Niemann-Pick C disease by RNA interference.

Rodriguez-Pascau L, Coll MJ, Casas J, Vilageliu L, Grinberg D.

JIMD Rep., 4, 29–37, 2012

C6-Ceramide and targeted inhibition of acid ceramidase induce synergistic decreases in breast cancer cell growth.

Flowers, M.; Fabrias, G.; Delgado, A.; Casas, J.; Abad, J. L.; Cabot, M. C.

Breast Cancer Res Treat, 133, 447–458, 2012

Sphingolipid modulation: a strategy for cancer therapy

Delgado A, Fabriàs G, Bedia C, Casas J, Abad JL.

Anticancer Agents MedChem 12, 285-302, 2012.

A lovastatin-elicited genetic program inhibits M2 macrophage polarization and enhances T cell infiltration into spontaneous mouse mammary tumors.

Mira E, Carmona-Rodríguez L, Tardáguila M, Azcoitia I, González-Martín A, Almonacid L, Casas J, Fabriás G, Mañes S.

Oncotarget., 4(12), 2288-301, 2013

Quantification of major urinary metabolites of PGE2 and PGD2 in cystic fibrosis: Correlation with disease severity.

Jabr S, Gartner S, Milne GL, Roca-Ferrer J, Casas J, Moreno A, Gelpí E, Picado C.

Prostaglandins, Leukotrienes Essential Fatty Acids, 89, 121-126, 2013

Straightforward access to spisulosine and 4,5-dehydrospisulosine stereoisomers: probes for profiling ceramide synthase activities in intact cells.

Abad JL, Nieves I, Rayo P, Casas J, Fabrias G, Delgado A.

J. Org. Chem., 78(12), 5858–5866, 2013

Systemic ceramide accumulation leads to severe and varied pathological consequences.

Alayoubi AM, Wang JC, Au BC, Carpentier S, Garcia V, Dworski S, El-Ghamrasni S, Kirouac KN, Exertier MJ, Xiong ZJ, Privé GG, Simonaro CM, Casas J, Fabriàs G, Schuchman EH, Turner PV, Hakem R, Levade T, Medin JA..

EMBO Mol. Med., 5(6), 827–842, 2013

Fat necrosis generates proinflammatory halogenated lipids during acute pancreatitis.

Franco-Pons N, Casas J, Fabriàs G, Gea-Sorli S, de-Madaria E, Gelpi E, Closa D.

Ann Surg, 257(5), 943-951, 2013.

Specific sphingolipid content decrease in Cerkl knockdown mouse retinas.

Garanto A, Mandal NA, Egido-Gabas M, Marfany G, Fabriàs G, Anderson RE, Casas J, Gonzalez-Duarte, R.

Exp. Eye Res., 110C, 96-106, 2013

Acid ceramidase as a therapeutic target in metastatic prostate cancer.

Camacho L, Meca-Cortes O, Abad JL, Garcia S, Rubio N, Diaz A, Celia-Terrassa T, Cingolani F, Bermudo R, Fernandez PL, Blanco J, Delgado A, Casas J, Fabriàs G, Thomson TM.

J. Lipid Res., 54(5), 1207-1220, 2013

Sphingolipid synthesis and scavenging in the intracellular apicomplexan parasite, Toxoplasma gondii.

Pratt S, Wansadhipathi-Kannangara NK, Bruce CR, Mina JG, Shams-Eldin H, Casas J, Hanada K, Schwarz RT, Sonda S, Denny PW.

Mol. & Biochem. Parasitology, 187(1), 43– 51, 2013

The nonlysosomal beta-glucosidase GBA2 promotes endoplasmic reticulum stress and impairs tumorigenicity of human melanoma cells.

Sorli SC, Colie S, Albinet V, Dubrac A, Touriol C, Guilbaud N, Bedia C, Fabriàs G, Casas J, Segui B, Levade T, Andrieu-Abadie N.

FASEB J, 27, 489-498, 2013.

Evaluation of phototransformation of antiviral zanamivir in surface waters through identification of transformation products.

Zonja, B.; Goncalves, C.; Perez, S.; Delgado, A.; Petrovic, M.; Alpendurada, M. F.; Barcelo, D.

J. Hazard. Mater. 2014, 265, 296–304.

Publications
(books and book chapters)

Natural Products as Platforms for the Design of Sphingolipid-Related Anticancer Agents.

Delgado A, Fabrias G, Casas J, Abad JL.
Advances in Cancer Research, Vol. 117C, Chapter 8, pp. 237-281. Burlington: Academic Press, 2013

Research projects

Dihidroesfingolipidos y autofagia en cancer. vias metabolicas y mecanismos moleculares implicados en la respuesta de las celulas tumorales a farmacos inductores de autofagia.

Nacional, SAF2011-22444

2012-2014

(E)-2-hexadecenal: un nuevo lípido bioactivo

Nacional, SAF2009-05589-E

2010-2012

Ayudas para apoyar las actividades de los grupos de investigación para el año 2009. Nombre del grupo: Reseach unit on bioactive molecules (RUBAM)

Generalitat, 2009SGR1072

2009-2014

Esfingolípids com a diana per a la recuperació de les lesions de la medul.la espinal: el paper de la esfingosina-1-fosfat.

Fundació La Marató de TV3

2012-2015

Análisis de lípidos

Bioibérica SA

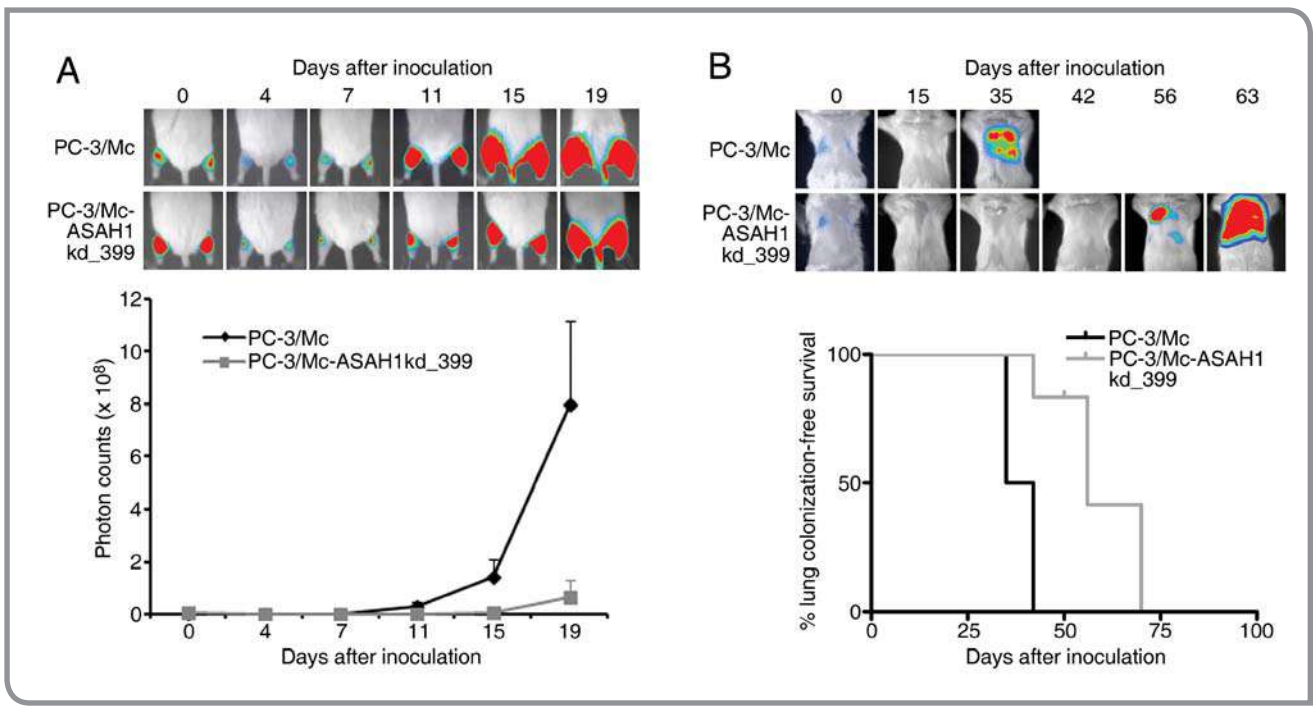
2013-2014.

Esfingolípidos poliénicos con fluorescencia latente: nuevas herramientas para el estudio de las propiedades biofísicas de las membranas celulares
Fundación Biofísica de Bizkaia

Research highlights

ACID CERAMIDASE AS A THERAPEUTIC TARGET IN METASTATIC PROSTATE CANCER.

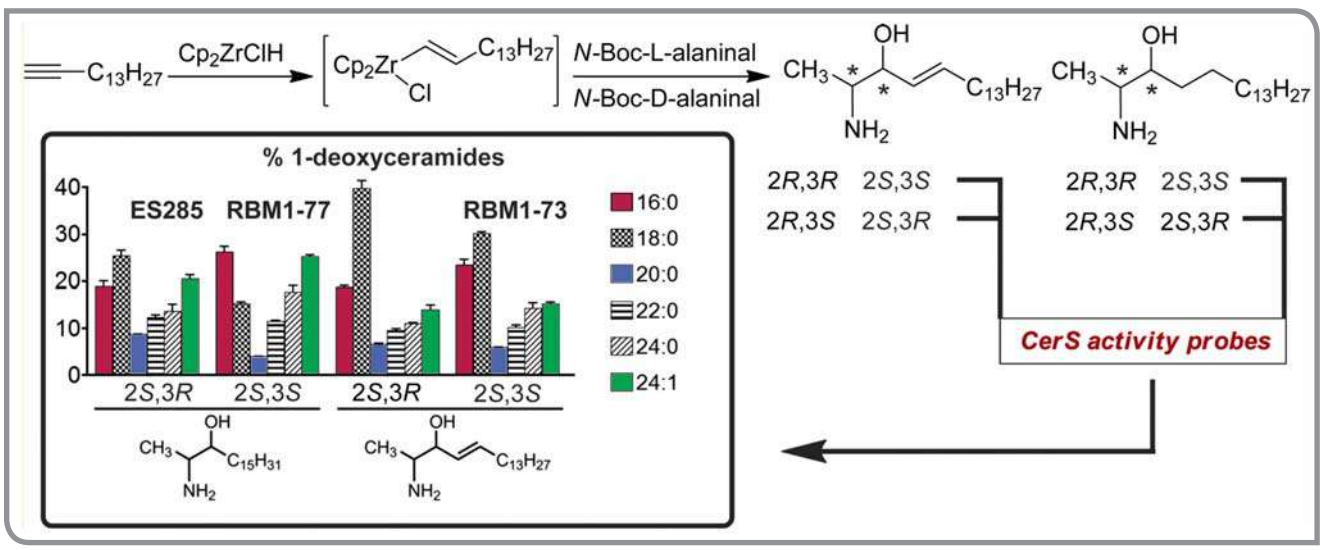
Acid ceramidase (AC) catalyzes the hydrolysis of ceramide into sphingosine, in turn a substrate of sphingosine kinases that catalyze its conversion into the mitogenic sphingosine-1-phosphate. AC is expressed at high levels in several tumor types and has been proposed as a cancer therapeutic target. Using a model derived from PC-3 prostate cancer cells, the highly tumorigenic, metastatic, and chemoresistant clone PC-3/Mc expressed higher levels of the AC ASAH1 than the nonmetastatic clone PC-3/S. Stable knockdown of ASAH1 in PC-3/Mc cells caused an accumulation of ceramides, inhibition of clonogenic potential, increased requirement for growth factors, and inhibition of tumorigenesis and lung metastases. We developed de novo ASAH1 inhibitors, which also caused a dose-dependent accumulation of ceramides in PC-3/Mc cells and inhibited their growth and clonogenicity. Finally, immunohistochemical analysis of primary prostate cancer samples showed that higher levels of ASAH1 were associated with more advanced stages of this neoplasia. These observations confirm ASAH1 as a therapeutic target in advanced and chemoresistant forms of prostate cancer and suggest that our new potent and specific AC inhibitors could act by counteracting critical growth properties of these highly aggressive tumor cells.



ASAH1 knockdown inhibits tumor growth and lung colonization of PC-3/Mc cells in NOD-SCID mice. A: Knock down of ASAH1 in PC-3/Mc cells with shRNA 399 strongly inhibits the growth of tumors. Controls were PC-3/Mc cells transduced with lentiviral particles carrying a LK0 vector expressing a nontargeting shRNA. Cells were inoculated intramuscularly in male NOD-SCID mice, and growth was monitored by bioluminescence. Upper panel: bioluminescent images of representative mice. Lower panel: Growth curves as a function of time (n = 8). B: Knockdown of ASAH1 in PC-3/Mc cells with shRNA 399 significantly delays lung colonization. Control cells were as in (A). Cells were inoculated intravenously in male NOD SCID mice, and lung colonization was monitored by bioluminescence. Upper panel: bioluminescent images of representative mice. Lower panel: Kaplan-Maier plots of lung colonization free-mice as a function of time (n = 8)

STRAIGHTFORWARD ACCESS TO SPISULOSINE AND 4,5 DEHYDRO-SPISULOSINE STEREOISOMERS: PROBES FOR PROFILING CERAMIDE SYNTHASE ACTIVITIES IN INTACT CELLS.

A stereoselective synthesis of spisulosine (ES285) and 4,5-dehydrospisulosine stereoisomers is described. Hydrozirconation of 1-pentadecyne with Schwartz reagent, followed by diastereocontrolled addition to L- or D-alaninal afforded the required 2-amino-1,3-diol framework. The resulting sphingoid bases revealed as excellent probes for the profiling of ceramide synthase activity in intact cells. Among the sphingoid bases described in this work, spisulosine (ES285), RBM1-77, and RBM1-73 were the most suitable ones because of their highest acylation rates. These molecules should prove useful to study the role of the different ceramide synthases and the resulting N-acyl (dihydro)ceramides in cell fate.



General synthetic approach to Spisulosine (ES285) and analogs thereof from N-Boc-L-alaninal and percentages of N-acylated species of the best ceramide synthase substrates amongst the different stereoisomeric spisulosines and analogs.

Synthesis and Biomedical Applications of Peptides

The Unit of Synthesis and Biomedical Applications of Peptides (USiBAP) interests focus on peptide chemistry from three different points of view: design, synthesis and therapeutic value of peptide molecules. The overall objectives of the USiBAP research summed up in the use of synthetic peptides in the field of Biomedicine both in improving diagnosis systems and in the design of new therapeutic targets. More specifically, work is being carried out on the design of immunopeptides, on the use of peptides for the development of new biosensors for the diagnosis of human illnesses and on the selection of therapeutic agents of peptide origin through biophysical testing.

STAFF
ISABEL HARO VILLAR, GROUP LEADER
MARIA JOSE GOMARA ELENA

TECHNICIANS
MARIA JOSE BLEDA HERNANDEZ
ANNA PAUS
RAYMOND ULLDEMOLINS

Ph. D. STUDENTS
LETICIA FERNANDEZ ARAUZO
RAMONA GALATOLA
AIMEE VASCONCELOS PACHECO

MASTER STUDENTS
MERITXELL COLOMER COLL

POST-GRADUATE STUDENTS
MARCO ALATI

TFG STUDENTS
MARTA TURU
MARCOS JIMENEZ
ALBA GRANADOS
DEBORA MARTINEZ
MARIA RICART

TECHNICIAN STUDENTS
ANA RODRIGUEZ
BEATRIZ SANZ DE MADRID
SARA LO-RE

Publications (articles)

Study of the interaction between the HIV-1 fusion peptide and E1/E2 GB virus C derived peptides.

Galatola, R., Gómara, M.J., Escarrà, M., Bleda, M.J., Pujol, M., Alsina, M.A., Haro, I.

Luminescence, 27, 540-542, 2012

Conjugation of peptides to PLGA-PEG nanoparticles incorporating flurbiprofen: in vitro drug release study.

Vasconcelos, A., Gómara, M.J., García, M.L., Haro, I.

Luminescence, 27, 571-572, 2012

Oligonucleotide-peptide conjugates: Solid-phase synthesis under acidic conditions and use in ELISA assays

Aviñó A, Gómara MJ, Malakoutikhah M, Haro I, Eritja R.

Molecules, 17(12), 13825-13843, 2012.

Physicochemical characterization of GBV-C E1 peptides as potential inhibitors of HIV-1 fusion peptide: Interaction with model membranes.

Sánchez-Martín, M.J.; Cruz, A.; Busquets, M.A.; Haro, I.; Alsina, M.A.; Pujol, M.

Int. J. Pharm., 436, 593– 601, 2012

Anti-citrullinated peptide antibodies in the serum of heavy smokers without rheumatoid arthritis. A differential effect of chronic obstructive pulmonary disease?.

Ruiz-Esquide V, Gómara MJ, Peinado VI, Gómez-Puerta JA, Barberà JA, Cañete J, Haro I, Sanmartí R.

Clin. Rheumatol., 31, 1047-1050, 2012

Synthetic peptides derived from an N-terminal domain of the E2 protein of GB virus C in the study of GBV-C/HIV-1 co-infection.

Fernández L, Chan WC, Egido M, Gómara MJ, Haro I.

J. Pept. Sci., 18, 326-335, 2012

Epifluorescence experiments to study GBV-C E1 peptides as potential inhibitors of HIV-1 fusion peptide: interaction with model membranes

Sánchez-Martín, M.J., Cruz, A., Busquets, M.A., Haro, I., Alsina, M.A., Pujol, M.

Luminescence, 27, 548-549, 2012

A morphological study of in vitro HIV-1 and E1(70-87) GBV-C peptide interaction by fluorescence microscopy

Ortiz, A., Fontvila, O., Muñoz, M., Busquets, M.A., Prat, J., Girona, V., Haro, I., Pujol, M.

Luminescence, 27, 549-551, 2012

Fluorescence analysis of the interaction of the peptide sequence E1(148-165) of GB virus C with liposomes

Sánchez-Martín, M.J., Pujol, M., Haro, I., Alsina, M.A., Busquets, M.A

Luminescence, 27, 552-553, 2012

Differences in synovial fluid cytokine levels but not in synovial tissue cell infiltrate between anti-citrullinated peptide/protein antibody-positive and -negative rheumatoid arthritis patients.

Gómez-Puerta JA, Celis R, Hernández MV, Ruiz-Esquide V, Ramírez J, Haro I, Cañete JD, Sanmartí R.

Arthritis Res Ther., 15(6), R182, 2013.

Contribution of the tyr-1 in plantaricin149a to disrupt phospholipid model membranes.

Lopes JL, Gómara MJ, Haro I, Tonarelli G, Beltramini LM.

Int J Mol Sci., 14(6), 12313-28, 2013

Citrullinated peptides in the diagnosis of rheumatoid arthritis.

Gómara MJ, Haro I.

Curr Top Med Chem.,13(6), 743-51, 2013.

Rheumatoid arthritis: current advances in pathogenesis, diagnosis and therapy (Editorial).

Haro I, Sanmartí R.

Curr Top Med Chem.,13(6), 697, 2013

Interaction of two overlapped synthetic peptides from GB virus C with charged mono and bilayers.

Alay M, Haro I, Alsina MA, Girona V, Prat J, Busquets MA.

Colloids Surf B Biointerfaces, 105, 7-13, 2013

Design and application of GB virus C (GBV-C) peptide microarrays for diagnosis of GBV-C/HIV-1 co-infection.

Fernández L, Bleda MJ, Gómara MJ, Haro I.

Anal Bioanal Chem., 405(12), 3973-82, 2013

Research Projects

Diseño, sintesis y estudio anti-HIV-1 de dominios peptidicos del GB virus C

Fundación para la Investigación del Sida en España (FIPSE), Ref 36-0735-09

Nacional, 2010-2013

Estudio estructural de dominios peptídicos del GB virus C con capacidad inhibitoria del HIV-1 y de aptámeros de RNA que se unen a la proteína PrP

Internacional, IT2009-0067

2010-2012

Péptidos sintéticos y nanosistemas derivatizados con construcciones peptídicas del GBV-C como potenciales agentes anti-HIV-1 y reactivos de diagnostico de infección por GBV-C

Nacional, CTQ2012-37589-C02-01

2013-2015

Reumatismo palindrómico: ¿entidad independiente o forma preclínica de artritis reumatoide? Papel de los anticuerpos frente a péptidos citrulinados

Nacional, Hospital Clínic

2013

Péptidos sintéticos en el estudio de la coinfección GBV-C/HGV y HIV-1

Nacional, CTQ2009-13969-C02-01

2010-2012

Multi-scale formation of functional nanocrystal-molecule assemblies and architectures

CCEE, 213382

2008-2012

Diseño de nanosistemas petidicos de liberacion controlada para la administracion ocular de farmacos

Internacional, 2011CU0003

2011-2015

Research highlights

DESIGN AND APPLICATION OF GB VIRUS C (GBV-C) PEPTIDE MICROARRAYS FOR DIAGNOSIS OF GBV-C / HIV-1 CO-INFECTION

The main objectives of the design of GBV-C peptide microarrays are the miniaturisation of antigen-antibody interaction assays, the simultaneous analysis of several peptide sequences and the reduction in the volume of serum required from patients, since this always represents a limiting factor in studies to develop new systems for diagnosing human diseases.

In this work we reported the design of a microarray immunoassay based on synthetic peptides derived from the GBV-C E2 protein to evaluate their diagnostic value in detecting anti-E2 antibodies in HIV-1 patients. To this end, peptide microarrays were initially prepared to identify the most relevant epitopes in the GBV-C E2 protein. Thus, 124 peptides composed of 18 amino acids covering the whole E2-protein sequence, with 15 residue overlaps, were spotted in triplicate onto γ-aminopropyl silane-functionalised adsorbent binding slides. The procedure to select the E2-protein epitopes was carried out using serum samples from HIV-1 infected patients. The samples had previously been tested for the presence or absence of GBV-C anti-E2 antibodies by means of the Abbott test. Thus, 11 specific epitopes in the GBV-C E2 protein were identified. Subsequently, peptide antigen microarrays were constructed using the E2 epitopes identified to detect GBV-C anti-E2 antibodies in the serum of HIV-1 infected patients with no known GBV-C co-infection. The 11 peptides selected identified anti-E2 GBV-C antibodies among HIV-1 infected patients and a reactivity of 47% was established. The potential antigenic peptides selected could be considered a useful tool for designing a new diagnostic system based on peptide microarrays to determine anti-GBV-C E2 antibodies in the serum of HIV-1 infected patients. Published in: Anal. Bioanal. Chem. 405, 3973-3982 2013,

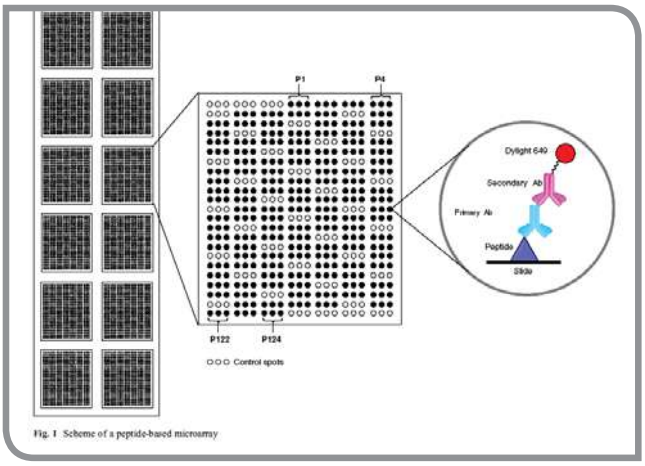
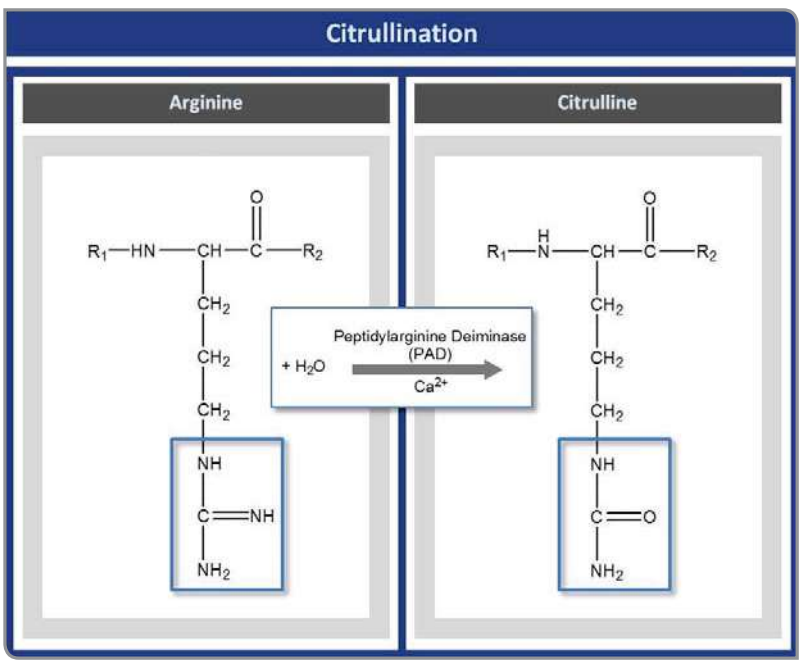


Fig. 1 Scheme of a peptide-based microarray

ANTI-CITRULLINATED PEPTIDE ANTIBODIES IN THE SERUM OF HEAVY SMOKERS WITHOUT RHEUMATOID ARTHRITIS. A DIFFERENTIAL EFFECT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE?

The objective of this study was to analyse the frequency and levels of anti-citrullinated peptide/protein antibodies (ACPA) in the serum of non-rheumatoid arthritis (RA) heavy smokers with and without chronic obstructive pulmonary disease (COPD) and compare them with healthy never smokers and patients with RA. Serum samples of 110 heavy smokers without RA, 209 healthy never smokers and 134 patients with RA were tested for ACPA using a commercial anti-cyclic citrullinated peptide antibodies (CCP2) test and a homemade chimeric fibrin/filaggrin citrullinated synthetic peptide (anti-CFFCP) ELISA test. The frequency of positive results and autoantibody levels were compared between groups. The prevalence of the two types of ACPA was slightly higher in heavy smokers than in never smokers, although the difference was not significant, and significantly lower than in RA patients. The highest prevalence of positive ACPA in heavy smokers was found in subjects with COPD (7.4% of positive anti-CFFCP in patients with COPD in comparison with 2.4% in never smokers: OR 3.26; 95% CI 0.85–12.6, p00.089). Mean serum levels of ACPA in heavy smokers were not significantly different from those of never smokers. Heavy smokers with COPD had significantly higher levels of anti-CFFCP than those without COPD, although almost all patients had serum levels below the cutoff values. The prevalence of ACPA in heavy smokers without RA is low, but seems to be higher in heavy smokers with COPD. Larger studies are necessary to confirm these findings and determine the relationship between ACPA and lung disease. Published in: Clin. Rheumatol. 31, 1047-1050, 2012.



Unit of Glycoconjugate Chemistry

The aim of the Unit is to study biochemical or medicinal chemistry issues by using chemical methodologies. Most frequently tools used are peptide and carbohydrate chemistry, halogenation reactions and aqueous organometallic catalysis. Traditional fields of interest are enzyme catalysis, pain and immunity related mechanisms and more recently, transthyretin amyloidosis inhibitors, Alzheimer disease interfering compounds and imaging diagnostics using radiotracers. Current research activities involve: 1) Study of pain and immunity related compounds. 2) Application of the iodinating reagent Ipy2BF4 to peptide and protein chemistry to effect further postsynthetic modifications. 3) Drug discovery for transthyretin related amyloid rare diseases. 4) Participation in radiotracer probes development for imaging diagnostics. All this activities are carried out in strong collaboration with computer design, biochemical, biological, pharmacological, conformational (NMR), crystallographic and nuclear chemistry groups at national and international level.

STAFF

GREGORIO VALENCIA PARERA, GROUP LEADER
GEMMA ARSEQUELL RUIZ

Ph. D. STUDENTS

MONICA ROSA EXPOSITO

Ph. D.

LLUÍS BOSCH HEREU

Publications (articles)

Methods to evaluate the inhibition of TTR fibrillogenesis induced by small ligands.

Arsequell G, Planas, A.

Curr. Med. Chem., 19(15), 2343-55, 2012.

Structure-activity relationship study of Opiorphin, a human dual ectopeptidase inhibitor with antinociceptive properties

Rosa M, Arsequell G, Rougeot C, Calle LP, Marcelo F, Pinto M, Centeno NB, Jiménez-Barbero J, Valencia, G.

J. Med. Chem., 55, 1181−1188, 2012.

Proposed bioactive conformations of opiorphin, an endogenous dual APN/NEP inhibitor.

Pinto M, Rougeot C, Gracia L, Rosa M, García A, Arsequell G, Valencia G, Centeno NB.

ACS Med. Chem. Lett. 3, 20−24, 2012.

Modulation of the fibrillogenesis inhibition properties of two transthyretin ligands by halogenation.

Cotrina EY, Pinto M, Bosch L, Vilà M, Blasi D, Quintana J, Centeno NB, Arsequell G, Planas A, Valencia G.

J Med Chem., 56(22), 9110-21, 2013.

Research projects

Activación química con metales y metaloides dirigida al acoplamiento C-C/C-heteroátomo y a la modificación de biomoléculas

Plan Nacional, CTQ2010-20517-C02-02

2011-2013

Desarrollo de nuevos fármacos para el tratamiento de la amiloidosis cardíaca relacionada con la transtiretina (Fundació La Marató TV3)2009-2014

Apoyo tecnológico sobre el ensayo clínico de referencia EC2009-012611-18

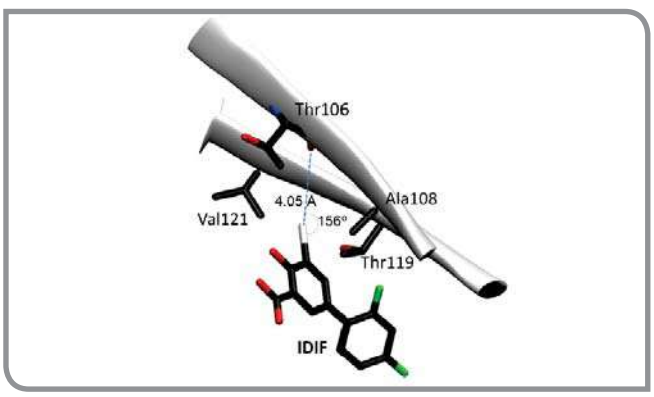
2013-2013

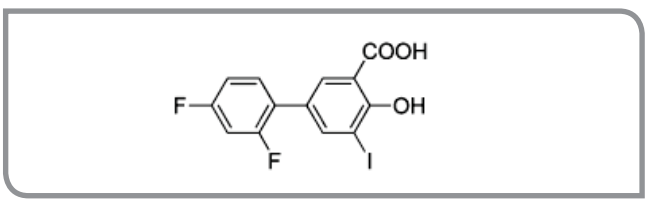
Síntesis purificación y caracterización de glicopéptidos
2012

Research highlights

Discovery of transthyretin amyloidosis inhibitors. With financial support from Fundació La Marató de TV3 (Grant No. 080530/31/32) we have continued a drug discovery effort initiated in year 2000 to find drug candidates for a group of rare diseases associated to transthyretin which is a thyroid hormone transporter protein. These systemic amyloid diseases are always triggered by single point hereditary mutations on the protein. The pharmacological intervention we are pursuing relies in small molecule compounds that bind to the binding pocked of thyroid hormones and in turn prevent the protein from dissociation from its tetrameric form and to further undergo misfolding and aggregation into amyloid deposits. Owing that thyroid hormones interact with the protein throughout "halogen binding pockets" we wanted to test the hypothesis that this sites may be used to create new "halogen bonds" that further stabilize the tetramer-ligand complexes. As a test compounds we have chosen two well-known transthyretin tetramer stabilizers, diflunisal and flufenamic acid, and synthesized two homologous series of halogenated derivatives and examined their binding affinities to the protein by calorimetric methods. Only in case of diflunisal a gradual increase of affinity going along the F, Cl, Br and I series was observed. By inspection of the transthyretin-iododiflunisal crystal structure this gradual increase could be assigned to a formation of a suboptimal halogen bonding between the ligand and the protein which confirmed that halogenation can be a design option when optimizing transthyretin-ligand interactions. These results were reported in J.Med. Chem. 56, 9110-9121, 2013.

Studies on antinociceptive compounds. On a project funded by Fundació La Marató 2006 we started the study of a recently discovered pain-related molecule called opiorphin which is a dual inhibitor of the ectopeptidases neprilysin (NEP) and aminopeptidase N (APN) that metabolizes a number of neuropeptides among them the enkephalins. Opiorphin produces analgesia in humans by inhibiting the enkephalin degradation. On a first SAR study of opiorphin, an Ala-scanning of its sequence has probed that Phe3 is a key residue for it dual enzyme inhibition properties. A more extensive examination of the role of Phe3 by a series of substitutions and derivatizations it was found that a L-Phe3 by D-Phe3 substitution increased APN inhibition potency of opiorphin by one order of magnitude while depleting NEP activity. Comparative conformational studies in solution by NMR and molecular mechanics calculations have shown that the observed potency enhancement may be due to the presence of π cation interactions between the aromatic ring of Phe3 and the guanidinium moiety of Arg2 that are only possible on the D-Phe3 analogue. In addition of gaining APN activity such L-Phe by D-Phe replacement strategy on opiorphin may also be useful for producing more metabolically stable analogues (J. Med. Chem. 55, 1181-1188, 2012). Simultaneously, we have been working on a computer model of the bioactive conformations that opiorphin adopts when binding to NEP and APN. For this we have used an iterative simulated annealing approach to generate a library of low-energy conformers that were pairwise faced to a set of experimental data from a small group of opiorphin sequences. The model obtained confirms that the inborn flexibility of opiorphin is essential of its analgesic properties (ACS Med. Chem. Lett. 3, 20-24, 2012).





Iododiflunisal

Figure: TTR-iododiflunisal complex.

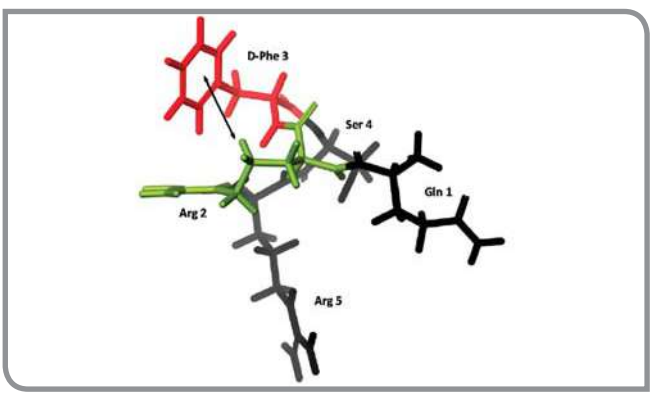


Figure: Model structure of the [D-Phe3]-opiorphin peptide showing the eventual interaction between the Hγ protons of Arg2 (in green) and D-Phe3 (in red).

Chemical Biology

Chemical biology is a discipline that applies chemical tools to investigate biological phenomena. Major advances have been seen in biology in the last decade thanks to the application of chemical biology strategies ranging from the synthesis of small molecule modulators of enzymes or protein-protein interactions to the design of new fluorophores, the establishment of new methods for target identification or the development of novel techniques in protein chemistry, among many others.

Our main objective in this field is the development of chemical tools that can contribute to the elucidation of the factors regulating diseases and to get a better understanding of relevant biological processes, with a special focus on autophagy. As a consequence, our research interests cover various fields of organic chemistry, biochemistry, molecular biology, biophysics and medicinal chemistry, thereby focusing on screen development, design and synthesis of small-molecule inhibitors, the establishment of novel strategies for peptide and protein chemistry, including protein synthesis, modification and immobilization, and the characterization of lipid-protein interactions.

STAFF

GEMMA TRIOLA, GROUP LEADER

Ph. D. STUDENTS

MIREIA QUINTANA

UNDERGRADUATE STUDENTS

ANA GUILLÉN
PHILIPP WOLF

VISITING STUDENT

KRISTINA LANG

Publications (articles)

Chemical-Biological Exploration of the Limits of the Ras De- and Repalmitoylating Machinery

Gormer, K.; Burger, M.; Kruijtzer, J. A. W.; Vetter, I.; Vartak, N.; Brunsveld, L.; Bastiaens, P. I. H.; Liskamp, R. M. J.; Triola, G.; Waldmann, H.

ChemBioChem 13, 1017-1023, 2012

N-Ras forms dimers at POPC membranes.

Guldenhaupt, J.; Rudack, T.; Bachler, P.; Mann, D.; Triola, G.; Waldmann, H.; Kotting, C.; Gerwert, K.

Biophys. J. 103, 1585-93, 2012

Revealing conformational substates of lipidated N-Ras protein by pressure modulation.

Kapoor, S.; Triola, G.; Vetter, I. R.; Erlkamp, M.; Waldmann, H.; Winter, R.

Proc Natl Acad Sci U S A 109, 460-5, 2012

The role of G-domain orientation and nucleotide state on the Ras isoform-specific membrane interaction.

Kapoor, S.; Weise, K.; Erlkamp, M.; Triola, G.; Waldmann, H.; Winter, R.

Eur. Biophys. J. 41, 801-13, 2012

Chemical biology of lipidated proteins.

Triola, G.; Waldmann, H.; Hedberg, C.

ACS Chem. Biol. 7, 87-99, 2012

Dissociation of the K-Ras4B/PDEdelta complex upon contact with lipid membranes: membrane delivery instead of extraction.

Weise, K.; Kapoor, S.; Werkmuller, A.; Mobitz, S.; Zimmermann, G.; Triola, G.; Waldmann, H.; Winter, R.

J. Am. Chem. Soc. 134, 11503-10, 2012,

Direct immobilization of oxyamine-modified proteins from cell lysates

Yi, L.; Chen, Y. X.; Lin, P. C.; Schroder, H.; Niemeyer, C. M.; Wu, Y. W.; Goody, R. S.; Triola, G.; Waldmann, H.
Chem Commun (Camb) 48, 10829-31, 2012.

Synthesis of lipidated peptides

Rosi, F.; Triola, G.

Methods Mol Biol 1047, 161-89, 2013,

Gibbs energy determinants of lipoprotein insertion into lipid membranes: the case study of Ras proteins.

Weise, K.; Huster, D.; Kapoor, S.; Triola, G.; Waldmann, H.; Winter, R

Faraday Discuss 161, 549-61; discussion 563-89, 2013,

Rotational and translational dynamics of ras proteins upon binding to model membrane systems

Werkmuller, A.; Triola, G.; Waldmann, H.; Winter, R.: Chemphyschem: a European journal of chemical physics and physical chemistry 14, 3698-705, 2013,

Semisynthetic lipidated LC3 protein mediates membrane fusion.

Yang, A.; Li, Y.; Pantoom, S.; Triola, G.; Wu, Y. W.: ChemBioChem 14, 1296-300, 2013,

Small molecule inhibition of the KRAS-PDEdelta interaction impairs oncogenic KRAS signalling.

Zimmermann, G.; Papke, B.; Ismail, S.; Vartak, N.; Chandra, A.; Hoffmann, M.; Hahn, S. A.; Triola, G.; Wittinghofer, A.; Bastiaens, P. I.; Waldmann, H.: Nature, 497, 638-642, 2013

Research Projects

Chemical biology of autophagy (PEOPLE-CIG/2914)

Career Integration Grants, Marie Curie Actions

01/2014 – 31/2017

Max-Planck Partner Group for Chemical Biology

Max Plank Gesellschaft

05/2014 – 04/2017

Desarrollo de inhibidores de Atg4B como inhibidores selectivos de autofagia (CTQ2013-44334-P) PN2013 – Proy. I+D – S.E.G.C.-P. Excelencia

01/2014-12/2016

Research highlights

BIOORTHOGONAL REACTIONS FOR SITE-SELECTIVE IMMOBILIZATION OF PROTEINS FROM CELL LYSATES

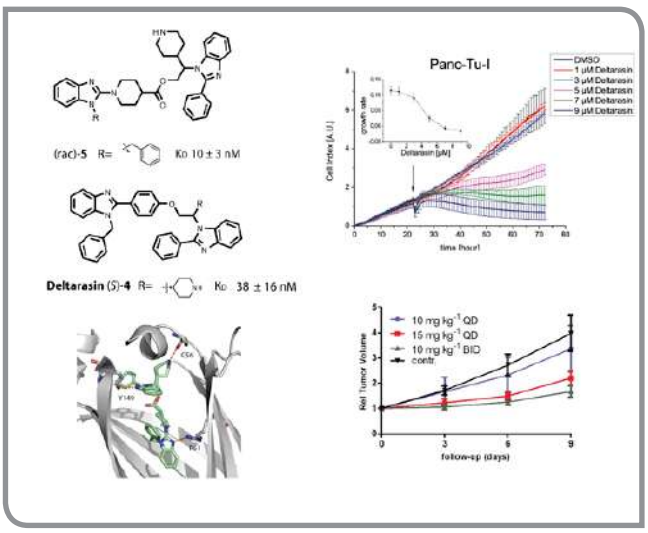
The immobilization of proteins on surfaces plays an important role in various areas of life science. The structural sensitivity of proteins calls for chemical transformations that proceed under mild conditions and are compatible with all their functional groups. Hence, the development of operationally simple and practical, and general techniques for the immobilization of functional proteins on solid supports remains a central challenge. In our work published in Chem Commun (Camb) 2012, 48, 10829-31, we report a new strategy for the immobilization of proteins based on oxime ligation. This facile, efficient and mild strategy employs proteins that are first modified with oxyamine groups at the C-terminus and then immobilized on ketone-coated slides to generate protein microarrays, which can be further used to study protein–protein interactions. Furthermore, this strategy enables the direct immobilization of expressed proteins from crude cellular lysates at neutral conditions (pH 7.0) and is exceptionally mild for protein immobilization. The produced protein biochips can be used for the study of protein– protein interactions, as indicated by Rab–REP and PKA–antibody interaction studies.

SMALL MOLECULES ABLE TO BLOCK ONCOGENIC RAS SIGNALING

Ras proteins are involved in many cellular processes regulating cell proliferation and differentiation. As a result, mutated Ras proteins leading to uncontrolled cell growth can be found in 30% of all cancers. For a correct localization and function, Ras proteins require proper membrane association and a precise localization. However, the molecular mechanisms regulating the cellular distribution of these proteins, i.e. the involvement of membrane diffusion processes or transport proteins, were largely unexplored**.**

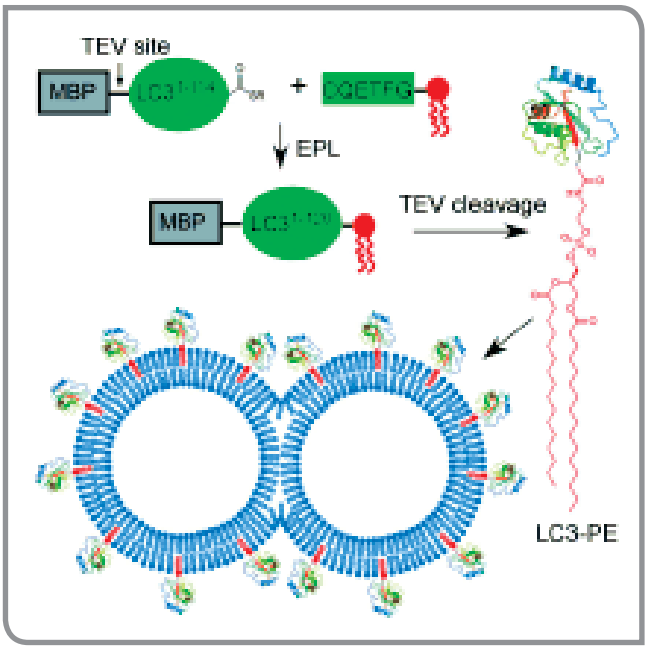
The KRAS oncogene product is considered a major target in anti-cancer drug discovery. However, direct interference with KRAS signalling has not yet led to clinically useful drugs. Correct localization and signalling by farnesylated KRAS is regulated by the prenyl-binding protein PDEd which sustains the spatial organization of KRAS by facilitating its diffusion in the cytoplasm. Here we report that interfering with binding of mammalian PDEd to KRAS by means of small molecules provides a novel opportunity to suppress oncogenic RAS signalling by altering its localization to endomembranes. Biochemical screening and subsequent structure-based hit optimization yielded inhibitors of the KRAS–PDEd

interaction that selectively bind to the prenyl-binding pocket of PDEd with nanomolar affinity, inhibit oncogenic RAS signalling and suppress in vitro and in vivo proliferation of human pancreatic ductal adenocarcinoma cells that are dependent on oncogenic KRAS. Our findings may inspire novel drug discovery efforts aimed at the development of drugs targeting oncogenic RAS. (*Nature* **2013**, *497*, 638-642).



SYNTHESIS OF A FULLY LIPIDATED LC3 PROTEIN

LC3 has been used as a bona fide marker of autophagosome and autophagy progression. Importantly, for a correct localization and activity, LC3 needs to be C-terminally modified with phosphatidylethanolamine. Despite the essential role of LC3 in autophagy, the molecular mechanisms regulating LC3 function are still unclear due to the lack of appropriate tools. In a recent work (Chembiochem. 2013;14(11):1296-300), we described the synthesis of a fully lipidated LC3 using a combination of lipidated peptide synthesis and expressed protein ligation. The resulting semisynthetic protein, C-terminally conjugated to a phosphatidylethanolamine, turn out to be an invaluable tool to investigate LC3 role in membrane tethering and fusion. The results obtained show that LC3 is able to promote membrane tethering and fusion at physiologically relevant PE concentrations. We are convinced that the employment of chemical biology strategies as the one described here will strongly contribute to expand our current knowledge of autophagy



Medicinal Chemistry

The Laboratory of Medicinal Chemistry (MedChemLab) is devoted to the discovery of small molecules with activity on biologically relevant processes, including medicinal chemistry and chemical biology. These include glycomimetics, enzyme inhibitors and light-operated ligands for optical control of proteins. The group has project in neurosciences (metabotropic glutamate receptors), glycolipids (immunology of NKT cells and metabolic rare diseases) and industry collaborative projects in drug discovery and synthesis. The research conducted includes the design and synthesis of molecules for multidisciplinary collaborative projects with groups of the biological, pharmaceutical and biophysical fields.

STAFF

AMADEU LLEBARIA SOLDEVILA, GROUP LEADER

Ph. D.

CARME SERRA
YOUSSEF HARRAK

Ph. D. STUDENTS

ANA TRAPERO
ANNA ALCAIDE
JOAN FONT
XAVIER GOMEZ-SANTACANA
TASSILO VOGEL
ESTER MONLLEÓ
ROSER BORRÀS

Publications (articles)

A prospect for pyrrolidine iminosugars as antidiabetic a-glucosidase inhibitors.

Trapero A, Llebaria, A.

J. Med. Chem., 55, 10345-10346, 2012.

Potent aminocyclitol glucocerebrosidase inhibitors are subnanomolar pharmacological chaperones for treating Gaucher disease.

Trapero A, González-Bulnes P, Butters TD, Llebaria A.

J. Med. Chem., 55, 4479–4488, 2012

Synthesis of 1-thio-phytosphingolipid analogs by microwave promoted reactions of thiols and aziridine derivatives.

Alcaide A, Llebaria A.

Tetrahedron Lett, 53, 2137–2139, 2012

Structural and functional characterization of a novel nonglycosidic type I NKT agonist with immunomodulatory properties

Kerzerho J, Yu ED, Barra CM, Alari-Pahissa E, Girardi E, Harrak Y, Lauzurica P, Llebaria A, Zajonc DM, Akbari O, Castaño AR.

J. Immunol. 188 , 2254-2265, 2012

Adamantane substituted aminocyclitols as pharmacological chaperones for Gaucher disease.

Trapero A, Egido-Gabás M, Llebaria A.

Med. Chem. Commun., 4, 1584-1589, 2013

Glucocerebrosidase inhibitors for the treatment of Gaucher disease.

Trapero A, Llebaria A.

Future Medicinal Chemistry, 5, 573-590, 2013

Research Projects

Estudios sobre la separación y purificación de glicolípidos de interés terapéutico

Nacional, 201280E128

2012

Ciclitoles como miméticos de carbohidratos y sus efectos en glicoenzimas y activación de células NKT por glicolípidos

Nacional, CTQ2011-29549-C02-01

2012-2014

pH controlled pharmacological chaperones

Nacional, CTQ2011-14868-E

2012-2014

Preparation of aminocyclitol substituted ceramides

Nacional, 201080E111

2010-2013

Validació de mglu4 com a diana terapeutica pel tractament multipotencial de les lesions medul.lars

Fundacio La Marato de TV3

2012-2015

Síntesis de nuevas moléculas fotoconmutables

IBEC

2011-2013

Development of light-modulated allosteric ligands of mglur4 for remote, non-invasive regulation of neuropathic pain.

IBEC

2011-2012

Estudios para el desarrollo de nuevos agentes antiinfecciosos

Omnia Molecular, S.L.

2009-2012

Desarrollo de síntesis de diferentes principios activos y sus impurezas

Interquim, S.A.

2012-2013

Síntesis de Gliptinas

Interquim, S.a.

2013-2014

Research Highligths

AMINOCYCLITOLS AS PHARMACOLOGICAL CHAPERONES IN GAUCHER DISEASE.

Different moleculescontaining the aminoaminocyclitol core have been synthesized and tested against glucocerebrosidase, the defective enzyme in Gaucher disease, with the aim of identifying pharmacological chaperones of further therapeutic usefulness.

Some of the compounds, having an aminocyclitol N-alkyl substituent have shown biochemical data similar or superior to those reported for N-nonyldeoxinojirimicyn, the reference compound. Amino-myo-inosito and their diamino derivatives have been found to be potent inhibitors of glucocerebrosidase (GCase), the β-glucosidase enzyme deficient in Gaucher disease (GD). The most potent inhibitors are also active in human fibroblast cell culture. When tested using lymphoblasts derived from patients with GD homozygous for N370S or L444P mutations, the compounds enhanced GCase activity at very low concentrations. These aminocyclitols produced maximum increases of GCase activities 40-90 in N370S and L444P lymphoblasts at nanomolar or subnanomolar concentrations. These results show that, in addition to inhibitory potency, this compound has the permeability, subcellular distribution, and cell metabolism characteristics that are important for use as a pharmacological chaperone. It is a remarkable finding that picomolar concentrations of aminocyclitols are sufficient to enhance activity in the L444P variant, which produces a severe neuronopathic form of GD without clinical treatment.

increases of GCase activities of 60% in N370S lymphoblasts at 100 nM and 30% in L444P at 1 nM

following a 3-day incubation, showing the permeability, subcellular distribution, and cell metabolism characteristics for use as pharmacological chaperone.

IMMUNOMODULATORY AGENTS

Research has been progressed on α-galactosylceramide (αGC) nonglycosidic analogues bearing galacto-configured aminocyclitols as sugar surrogates have been obtained. Natural Killer T (NKT) cellular assays have resulted in the identification of an active compound able to promote NKT cell expansion in vitro in a similar fashion but more weakly than αGC in vitro, although in vivo it induces robust IFN-γ production, and highly reduced but still functional Th2 response. The characteristic cytokine storm produced upon α-GalCer activation was not induced. Consequently, HS44 a prototypical aminocyclitol molecule, induces very efficient iNKT cell-dependent antitumoral response in B16 animal model. In addition, intranasal administration shows the capacity to induce lung inflammation and airway hyperreactivity, a cardinal asthma feature. Thus, HS44 is able to elicit functional Th1 or Th2 responses. Structural studies show that HS44 binds to CD1d with the same conformation as α-GalCer. The proteins bind to HS44 similarly as α-GalCer, but forms less contacts, thus explaining its weaker TCR affinity and, consequently, its weaker recognition by iNKT cells. The ability of this compound to activate an efficient, but not massive, tailored functional immune response makes it an attractive reagent for immune manipulation.

Overall, these data confirm the agonist activity of αGC lipid analogues having charged amino-substituted polar heads and their capacity to modulate the response arising from iNKT cell activation in vivo.

4

Department of Chemical and Biomolecular Nanotechnology

Department of Chemical and Biomolecular Nanotechnology

Heads: Mª Pilar Marco Colàs / Jordi Esquena Moret

Research at the Chemical and Biomolecular Nanotechnology Department is focused on bioactive organic molecules and biomolecules, nanomaterials and devices and self-organized supramolecular or colloidal systems. Thus, the research groups of the department hold a great expertise on the chemistry of bioactive substances and their preparation using combinatorial chemistry tools, designing and screening virtual libraries. Knowledge on the chemistry of oligonucleotides allows to rationally synthesize molecules with affinity to dsDNA and G-quadruplex as well as to design new nucleic acid derivatives to control gene expression by antisense and RNA interference mechanisms. The capability to produce antibodies, natural molecules with inherent capabilities to specifically react with their counter antigen, and to direct their features according to the needs, allows designing bioreceptors for a wide range of applications. The integration of these biomolecules with certain micro(nano)materials and devices with unique physical properties allows developing novel biosensors with improved features envisaging a new generation of molecular diagnostic tools useful in the clinical and food safety fields. Finally, and regarding the preparation of new nanostructures, the expertise acquired for many years on the chemistry of the surfactants and their capability to self-aggregate to form complex supramolecular structures (micelles, liquid crystals, microemulsions, nano-emulsions, highly concentrated emulsions, etc.) has lead to investigate their use as templates for the preparation of new nanostructured materials (organic, inorganic, hybrid) with controlled size and morphology as well as new drug delivery systems.

Research groups

- Nanobiotechnology for Diagnostics
- Nucleic Acids Chemistry
- Colloid and Interfacial Chemistry
- Cell Therapy
- Surface Chemistry

Nanobiotechnology for Diagnostics

The Nanobiotechnology for Diagnostics Groupe, formerly Applied Molecular Receptors Group (AMRg) has focussed on the development of novel molecular diagnostic tools to provide alternatives to the actual limitations existing in several fields, but particularly in the clinical and food safety areas. The combination of nanotechnological and biotechnological advances has given raise to novel molecular diagnostic approaches to improve efficiency and/or to refine and extend the limits of detection. Nanostructured surfaces and nanoparticles may be the base for the construction of functional hybrid materials consisting of both organic (biomolecules) and inorganic components. Biosensors are between the potential applications of these new immunosensors using antibodies as biorecognition elements displaying fascinating features such as the possibility to respond selectively to biological or bio-active substances and the capability to respond in a physiological manner. The unique properties of certain nanomaterials combined with the excellent features of the antibodies allow envisaging novel exquisitely sensitive chemical and biological sensors.

STAFF

M.PILAR MARCO COLÁS, GROUP LEADER
ROGER GALVE BOSCH
FRANCISCO SÁNCHEZ BAEZA
NÚRIA PASCUAL DURAN

TECHNICIANS

MARTA RUIZ ARRIBAS
ANA GONZALEZ GONZALEZ

Ph. D.

J.PABLO SALVADOR VICO
ENRIQUE VALERA CANO
MONTSERRAT RODRÍGUEZ NÚÑEZ
LORENA GARCIA FERNANDEZ

Ph. D. STUDENTS

DANIEL GONZÁLEZ PINACHO
GLORIA COLOM SANMARTÍ
RAUL GARCIA FEBRERO
CARME PASTELLS DÍEZ
SALVADOR PETANÁS ESTEBAN
ESTER VILA ROCA
ALEX HERNANDEZ ALBORS
NURIA TORT ESCRIBÀ
SÓNIA MATAS MOYA
ALEJANDRO MURIANO CASTAÑÓN

MASTER STUDENTS

MARTA BROTO AVILES
RUTH BABINGTON
DIANA NAVARRO MOSLAN

Publications (articles)

Two-photon fluorescent immunosensor for androgenic hormones using resonant grating waveguide structures.

Muriano A, Thayil KNA, Salvador J-P, Loza-Alvarez P, Soria S, Galve R, Marco MP.
Sensors and Actuators B: Chemical, 174(0), 394-401, 2012

Design and fabrication of a COP-based microfluidic chip: chronoamperometric detection of troponin T.

Abad L, Javier del Campo F, Muñoz FX, Fernández LJ, Calavia D, Colom G, Salvador JP, Marco MP, Escamilla-Gómez V, Esteban-Fernández de Ávila B, Campuzano S, Pedrero M, Pingarrón JM, Godino N, Gorkin R 3rd, Ducrée J.
Electrophoresis, 33(21), 1–8, 2012

Molecular modeling assisted hapten design to produce broad selectivity antibodies for fluoroquinolone antibiotics.

Pinacho DG, Sánchez-Baeza F, Marco MP.
Anal. Chem., 84(10), 4527-4534, 2012

Current bioanalytical methods for detection of penicillins.

Babington R, Matas S, Marco M-P, Galve R.
Anal. Bioanal. Chem., 403(6), 1549-1566, 2012

Preparation of antibodies and development of an Enzyme-Linked Immunosorbent Assay (ELISA) for the determination of doxycycline antibiotic in milk samples.

Adrian J, Fernández F, Sánchez-Baeza F, Marco MP.
J. Agric. Food Chem., 60(15), 3837-3846, 2012

Disposable and integrated amperometric immunosensor for direct determination of sulfonamide antibiotics in milk.

Conzuelo F, Gamella M, Campuzano S, Pinacho D, Reviejo AJ, Marco MP, Pingarrón JM.
Biosensors and Bioelectronics, 36(1), 81-88, 2012

Multiplexed immunoassay to detect anabolic androgenic steroids in human serum.

Tort N, Salvador J-P, Marco MP.
Anal. Bioanal. Chem., 403, 1361-1371, 2012

Nanogold probe enhanced Surface Plasmon Resonance immunosensor for improved detection of antibiotic residues.

Fernández F, Sánchez-Baeza F, Marco MP.
Biosensors and Bioelectronics, 34, 151–158, 2012

Development of an immunoassay for terbutryn: Study of the influence of the immunization protocol.

Sanvicens N, Varela B, Ballesteros B, Marco MP.
Talanta 89, 310–316, 2012

Three-Dimensional Interdigitated Electrode Array as a Tool for Surface Reactions Registration.

Bratov A, Abramova N, Marco MP, Sanchez-Baeza F.
Electroanalysis, 24(1), 69–75, 2012

Synthesis of steroid-oligonucleotide conjugates for a site-encoded SPR immunosensor

Tort N, Salvador JP, Aviñó A, Eritja R, Comelles J, Martínez E, Samitier J, Marco MP.
Bioconjug. Chem., 23(11) 2183-2191, 2012.

Bond Elasticity Controls Molecular Recognition Specificity in Antibody–Antigen Binding.

Alemany A, Sanvicens N, de Lorenzo S, Marco MP, Ritort F.
Nano Lett., 13(11), 5197–5202, 2013.

A portable electrochemical magnetoimmunosensor for detection of sulfonamide antimicrobials in honey.

Muriano A, Pinacho DG, Chabottaux V, Diserens JM, Granier B, Stead S, Sanchez Baeza F, Pividori MI, Marco MP.
Anal. Bioanal. Chem., 405(24), 7885-7895, 2013

An electrochemical magneto immunosensor (EMIS) for the determination of paraquat residues in potato samples.

Garcia-Febrero R, Valera E, Muriano A, Pividori MI, Sanchez-Baeza F, Marco MP.
Anal. Bioanal. Chem., 405(24), 7841-7849, 2013

Ultrasensitive amperometric magnetoimmunosensor for human C-reactive protein quantification in serum.

Esteban-Fernández de Ávila B, Escamilla-Gómez V, Campuzano S, Pedrero M, Salvador JP, Marco MP, Pingarrón JM.
Sensors and Actuators B, 188, 212– 220, 2013

Integrated disposable electrochemical immunosensors for the simultaneous determination of sulfonamide and tetracycline antibiotics residues in milk.

Conzuelo F, Campuzano S, Gamella M, Pinacho DG, Reviejo AJ, Marco MP, Pingarrón JM.
Biosensors and Bioelectronics, 50, 100–105, 2013.

Development of a Coulombimetric immunosensor based on specific antibodies labeled with CdS nanoparticles for sulfonamide antibiotic residues analysis and its application to honey samples.

Valera E, Muriano A, Pividori I, Sánchez-Baeza F, Marco MP.
Biosensors and Bioelectronics, 43, 211–217, 2013.

Publications
(books and book chapters)

Nanobiosensors for in vitro and in vivo analysis of biomolecules

Salvador JP, Kreuzer MP, Quidant R, Badenes G, Marco MP.

Methods in Molecular Biology, Vol. 811, 207-221, 2012.

"Nanotechnology Regenerative Medicine: Methods and Protocols. (J.A. Planell, M. Navarro Eds.) Humana Press, Springer, New York.

Application of bioassays/biosensors for the analysis of pharmaceuticals in environmental samples.

Valera E, Babington R, Broto M, Petanas S, Galve R, Marco MP.

Comprehensive Analytical Chemistry, Vol. 62, 195-229, 2013 in Analysis, removal, effects and risk of pharmaceuticals in the water cycle occurrence and transformation in the environment

(Petrovic M, Barceló D, Pérez S. Eds), Elsevier, B. V.

Research projects

Plataformas de diagnostico universal basadas en nanopartículas codificadas con oligonucleótidos y dispositivos de microarrays de DNA

Nacional, MAT2012-38573-C02-01
2013-2015

Electrochemical immunosensor system for the detection of neuroactive trytophan metabolites. Development of immunoreagents and nanostructured biohybrid sensing surfaces

Nacional, CTQ2011-29163-C03-01
2012-2014

Plataformas de diagnóstico universal basada en nanopartículas codificadas con oligonucleótidos y dispositivos de microarrays de DNA

Nacional, MAT2011-29335-C03-01
2012

Microcavidades ópticas para la detección de antibióticos y esteroides

Internacional, 2010IT0040
2011-2012

Chip Architectures by Joint Associated Labs for European Diagnostics

Nacional, PLE2009-0168. 2010-2013

To develop diagnostic products in accordance to the market needs and to guarantee a quick transfer of the results and release of products to the market

2011-2013

Preparation and characterization of new haptens (immunizing and competitor haptens) and immunoreagents (immunogens and coating antigens) for the immunochemical detection of kynurenine and kynurenic acid

2011-2012. Pharmasan Labs Inc.

Convenio entre el CSIC y el centro de investigacion biomedica en red de bioingenieria, biomateriales y nanomedicina - CIBER-BBN - para desarrollar las relaciones entre el CIBER-BBN y el CSIC

Principal Investigators: R. Eritja, C. Solans, M.P. Marco, J. Blanco
2010-2015

Nanotecnología para cardiología y neumococo (NanoCardioCoco)

Nacional IPT2011-1337-010000
2011-2014

Sistemas de detección y cuantificación de biomarcadores de la enfermedad de Alzheimer (KIT-Alzheimer)

Nacional IPT2011-1055-900000
2011-2014

Design and evaluation of a novel impedimetric immunosensor for the diagnosis of sepsis of respiratory origin due to Pseudomonas aeruginosa

Convenio CIBER-BBN/CIBERES/SEPAR
2013-2014

Test-kits for antibiotic detection

2010-2013. Unisensor, S.A.

Desarrollo de sistemas de monitorización de la exposición laboral a productos tóxicos.

2013-2015. Cotemmsa

Preparation and characterization of haptens and immunoreagents for the selective detection and quantification of kynurenine metabotic pathway

2013-2015. Pharmasan Labs Inc.

Desarrollo de anticuerpos mediante la utilización de péptidos sintéticos

2012-2014. Zeu Inmunotec, S.L.

Research highlights

The Nb4D group has continued to develop antibodies against molecules of interest in the food safety and clinical diagnosis fields. Examples of recent developments include the production of antibodies against cardiac biomarkers, cytostatic agents, neurological disease biomarkers and antibiotics.

An ELISA method for the detection of the banned pesticide paraquat has been developed as part of the European project Conffidence (KBBE2007-211326). The specific antibodies against paraquat were later labelled with CdS nanoparticles (CdSNP) and combined with antigen biofunctional magnetic µ-particles to create electrochemical nanoprobes which can be measured using graphite composite electrodes (GECs). After the immunochemical reaction the CdSNP are dissolved and the metal released are reduced at the electrode and read in the form of current or charge signal by an anodic stripping technique. Due to the amplification effect produced by the CdSNP on the amperometric/coloumbimetric signal a very high detectability is reached.

Electrochemical detection has also been employed to detect fluoroquinolone antibiotics. The amperometric magento-immunosensor (AMIS) combines magnetic beads biomodified with an antibody against the fluroquinolone family modity, a haptenised enzyme and a magnetic graphite-epoxy composite (mGEC) electrode. Also, the fluoroquinolone enrofloxacin has been successfully determined in hair samples by an ELISA method which is an attractive non-invasive alternative to control misuse of such antibiotic and to ensure food safety by preventing such food derived products arrive to the consumer.

The group is also collaborating with the TIR group and the Group on Clinical Microbiology and Experimental Infectious Pathology in the project NanBioSepRes. The main objective of which is the development and validation of an Impedimetric immunosensor platform that can be used for point of care (PoC) clinical diagnosis of Pseudomonas aeruginosa infections.

Three new patents have been deposited in the Spanish Office for Patents since 2012. These include P201230378 "Compounds derived from doxycycline such as haptens, conjugates and antibodies thereof and immunochemical method for detecting doxycycline", P201231836 "Antibodies for detecting and quantifying anticoagulant agents", and P201330312 "Haptens and conjugates derived from pyocycanin, antibodies thereof and immunochemical method for detecting infections caused by Pseudomonas aeruginosa". All three have had PCTs published. Other patents have extended to various countries including patent P201031721 which has been extended to the United States, Europe and China as well as having the PCT. This patent was licensed to Unisensor SA (Belgium) in 2012. Patent P200931164 which was licensed out to Thrombotargets Europe in 2011 has since been extended to the United States, Canada, Europe, China, Japan and Mexico.

A reproducible procedure for the preparation of well-defined and characterized gold nanoprobes has been established and their effect enhancing the detectability of Surface Plasmon Resonance (SPR) biosensors has been demonstrated.

Steroid-oligonucleotide bioconjugates have been synthesized and characterized for their use on DNA-directed immobilization of haptens on SPR sensors.

It has been demonstrated the possibility to use electrochemical nanoprobes for the amperometric detection of target markers at low concentration levels in complex samples.

A renovation for two years research collaboration agreement has been signed with Pharmasan Laboratories (WI, USA) for the development of new immunoreagents with diagnostic purposes.

The research collaboration contract with Unisensor (Liege, Belgium) for the development of immunoreagents has been renewed during the 2012-2013 period.

The website of the group has been launched. It can be found at www.iqac.csic.es/nb4d. The latest research news and career options can be found along with the scientific and technological offers of the group.

Finally, the Nanobiotechnology and Molecular Diagnostics group continues to work on new strategies for the screening of small organic molecules, including condumetric sensors, optical biosensors, quantum-dot based arrays, microarrays and the standard ELISA etc.

Nucleic Acids Chemistry

Synthetic oligonucleotides are convenient tools for a large number of studies. The aim of our group is the study of the methodology used for the synthesis of DNA and RNA derivatives in order to obtain new compounds with new and / or improved properties. The projects undertaken along 2012-2013 deal with 1) conjugation of small molecules to DNA and RNA for a potential use in DNA/ RNA therapeutics, 2) the effect of modified bases in the structural and biological properties of oligonucleotides, and 3) the use of modified oligonucleotides in the assembly of nanomaterials and biosensors.

STAFF

RAMON ERITJA CASADELLÀ, GROUP LEADER

Ph. D.

ANNA MARIA AVIÑÓ ANDRÉS
MARIA CARME FÀBREGA CLAVERÍA
SANTIAGO GRIJALVO TORRIJO
SONIA PÉREZ RENTERO
MONTSERRAT TERRAZAS MARTÍNEZ

Ph. D. STUDENTS

RUBEN FERREIRA
ADELE ALAGIA
MARIA TINTORÈ GASULLA

Publications (articles)

Functionally enhanced siRNA targeting TNFa attenuates DSS-induced colitis and TLR-mediated immunostimulation in mice

Ocampo, S.M., Romero, C., Aviñó, A., Burgueño, J., Gassull, M.A., Bermúdez, J., Eritja, R., Fernandez, E., Perales, J.C.

Mol. Ther. 20(2), 382-390, **2012**.

Thrombin binding aptamer, more than a simple aptamer: Chemically modified derivatives and biomedical applications

Aviñó, A., Fàbrega, C., Tintoré, M., Eritja, R.

Curr. Pharm. Design 18(14), 2036-2047, **2012**.

Synthesis and in vitro inhibition properties of siRNA conjugates carrying acridine and quindoline moieties

Aviñó, A., Ocampo, S.M., Perales, J.C., Eritja, R.

Chem. Biodivers. 9(3), 557-566, **2012**.

Sensitive and label-free biosensing of RNA with predicted secondary structures by a triplex affinity capture method

Carrascosa, L.G., Gómez-Montes, S., Aviñó, A., Nadal, A., Pla, M., Eritja, R., Lechuga, L.M.

Nucleic Acids Res. 40(8), e56, **2012**.

The structure of triplex DNA in the gas phase

Arcella, A., Portella, G., Ruiz, M., Eritja, R., Vilaseca, M., Gabelica, V., Orozco, M.
J. Am. Chem. Soc. 134(15), 6596-6606, **2012**.

Facile modification of silica substrates provides a platform for direct-writing surface click chemistry

Oberhansl, S., Hirtz, M., Lagunas, A., Eritja, R., Martínez, E., Fuchs, H., Samitier, J.
Small 8(4), 541-545, **2012**.

Apolar carbohydrates as DNA capping agents

Lucas, R., Vengut-Climent, E., Gómez-Pinto, I., Aviñó, A., Eritja, R., González, C., Morales, J.C.
Chem Comm. 48(24), 2991-2993, **2012**.

Synthesis and in vitro inhibition properties of oligonucleotide conjugates carrying amphiphatic proline-rich peptide derivatives of the sweet arrow peptide (SAP)

Grijalvo, S., Eritja, R.
Mol. Divers. 16(2), 307-317, **2012**.

Impact of methylation on the physical properties of DNA

Pérez, A., Castellazzi, C.L., Battistini, F., Collinet, K., Flores, O., Deniz, O., Ruiz, M. L., Torrents, D., Eritja, R., Soler-López, M., Orozco, M.

Biophys. J. 102(9), 2140-2148, **2012**.

Development of an impedimetric DNA-biosensor based on layered double hydroxide for the detection of long ssDNA sequences

Baccar, Z. M., Caballero, D., Eritja, R., Errachid, A.

Electrochim. Acta, 74, 123-129, **2012**.

Interstrand interactions on DNA duplexes modified by TTF units at the 3' or 5'-ends

Pérez-Rentero, S., Gállego, I., Somoza, A., Ferreira, R., Janousek, J., Belohradsky, M., Stara, I., Stary, I., Eritja, R.

RSC Adv. 2(10) 4069-4071, **2012**.

Synthesis and structural characterization of stable branched G-quadruplexes using the trebler phosphoramidite

Ferreira, R., Alvira, M., Aviñó, A., Gómez-Pinto, I., González, C., Gabelica, V., Eritja, R.

ChemistryOpen 1(2), 106-114, **2012**, doi: 10.1002/open.201200009

Synthesis, DNA-binding and anti-proliferative properties of acridine and 5-methylacridine derivatives

Ferreira, R., Aviñó, A., Mazzini, S., Eritja, R.
Molecules 17(6), 7067-7082, **2012**.

Synthesis of steroid-oligonucleotide conjugates for a site-encoded SPR immunosensor

Tort, N., Salvador, J.P., Aviñó, A., Eritja, R., Comelles, J., Martínez, E., Samitier, J., Marco, M.P.
Bioconjug. Chem. 23(11) 2183-2191, **2012**.

The effect on quadruplex stability of North-nucleoside derivatives in the loops of the thrombin-binding aptamer

Aviñó, A., Mazzini, S., Ferreira, R., Gargallo, R., Marquez, V. E., Eritja, R.

Bioorg. Med. Chem. 20(14), 4186-4193, **2012**.

Porphyrin binding mechanisms is altered by protonation at the loops in G-quadruplex DNA formed near the transcriptional activiation site of the human c-kit gene

Manaye, S., Eritja, R., Aviñó, A., Jaumot, J., Gargallo, R.

Biochim. Biophys. Acta-Gen. Subj, 1820(12), 1987-1996 2012.

Receptor-based virtual screening and biological characterization of human apurinic/ apyrimidinic endonuclease (Ape1) inhibitors

Ruiz, F.M., Francis, S.M., Tintoré, M., Ferreira, R., Gil-Redondo, R., Morreale, A., Ortiz, A.R., Eritja, R., Fàbrega, C.

ChemMedChem 7(12), 2168-2178, **2012**.

Synthesis of oligonucleotides carrying thiol groups using a simple reagent derived from threoninol

Pérez-Rentero, Grijalvo, S., Ferreira, R., Eritja, R.

Molecules 17(9), 10026-10045 , **2012**.

Oligonucleotide-peptide conjugates: Solid-phase synthesis under acidic conditions and use in ELISA assays

Aviñó, A., Gómara, M.J., Malakoutikhah, M., Haro, I., Eritja, R.

Molecules 17(12), 13825-13843, **2012**.

Mass spectrometry and ion mobility spectrometry of G-quadruplexes. A study of solvent effects on dimer formation and structural transitions in th etelomeric DNA sequence d(TAGGGTTAGGGT)

Ferreira, R., Marchand, A., Gavelica V.

Methods 57(1) 56-63, **2012**.

Functionalization of the 3'-ends of DNA and RNA strands with N-ethyl-N-coupled nucleosides: A promising approach to avoid 3'-exonuclease-catalyzed hydrolysis of therapeutic oligonucleotides

Terrazas, M., Alagia, A., Faustino, I., Orozco, M., Eritja, R.

ChemBioChem 14(4), 510-520, **2013**.

Structure and stability of human telomeric G-quadruplex with preclinical 9-amino acridines

Ferreira, R., Artali, R., Benoit, A., Gargallo, R., Eritja, R., Ferguson, D.M., Sham, Y.Y., Mazzini, S.

PLOS ONE 8(3), e57701, **2013**.

Carbohydrate DNA interaction at G-quadruplexes: folding and stability changes by attaching sugars at the 5'-end

Gómez-Pinto, I., Vengut-Climent, E., Lucas, R., Aviñó, A., Eritja, R., González, C., Morales, J.C.

Chem. Eur. J. 19(6), 1920-1927, **2013**.

Efficient self-assembly in water of long noncovalent polymers by nucleobase analogs

Cafferty, B.J., Gállego, I., Chen, M.C., Farley, K. I., Eritja, R., Hud, N. V.

J. Am. Chem. Soc. 135(7), 2447-2450, **2013**.

Double-tailed lipid modification as a promising candidate for oligonucleotide delivery in mammalian cells

Ugarte-Uribe, B., Grijalvo, S., Busto, J. V., Martín, C., Eritja, R., Goñi, F. M., Alkorta, I.

Biochim. Biophys. Acta-Gen. Subj. 1830(10), 4872-4884 **2013**.

Electrostatic binding and hydrophobic collapse of peptide-nucleic acid aggregates quantified using force spectroscopy

Camuñas-Soler, J., Frutos, S., Bizarro, C.V., de Lorenzo, S., Fuentes-Perez, M.A., Ramsch, R., Vilchez, S., Solans, C., Moreno-Herrero, F., Albericio, F., Eritja, R., Giralt, E., Dev, S.B., Ritort, F.

ACS Nano 6(7), 5102-5113, **2013**.

DNA Origami as DNA repair nanosensor at the single-molecule level

Tintoré, M., Gállego, I., Manning, B., Eritja, R., Fàbrega, C.

Angew. Chem. Int. Ed. Engl. 52(30) 7747-7750, **2013**.

An aptamer-gated silica mesoporous material for thrombin detection

Oroval, M., Climent, E., Coll, C., Eritja, R., Aviñó, A., Marcos, M.D., Sancenón, F., Martínez-Máñez, R., Amorós, P.

Chem. Comm. 49(48), 5480-5482, **2013**.

Self-assembled G-quadruplex nanostructures: AFM and voltammetric characterization

Chiorcea-Paquim, A.M., Santos, P., Eritja, R., Oliveira-Brett, A.

PhysChemPhysChem 15(23), 9117-9124, **2013**.

Synthesis, RNAi activity and nuclease-resistant properties of apolar carbohydrates siRNA conjugates

Vengut-Climent, E., Terrazas, M., Lucas, R., Arévalo-Ruiz, M., Eritja, R., Morales J.C.

Bioorg. Med. Chem Lett. 23, 4048-4051, **2013**.

Sequence and solvent effects on telomeric DNA bimolecular G-quadruplex folding kinetics.

Marchand, A., Ferreira, R., Tateishi-Karimata, H., Miyoshi, D., Sugimoto, N., Gabelica, V.
J. Phys. Chem. B 117(41), 12391-12401, **2013**.

Biophysical and RNA interference inhibitory properties of oligonucleotides carrying tetrathiofulvalene groups at terminal positions

Pérez-Rentero, S., Somoza, A., Grijalvo, S., Janousek, J., Belohradsky, M., Stara, I.G., Stary, I., Eritja, R.
Journal of Chemistry 2013, ID 650610, 11 pages **2013**; doi: 10.1155/2013/650610

Supramolecular polymerization of nucleobase-like monomers in water

Gállego, I., Cafferty, B.J., Chen, M.C., Farley, K.I., Eritja, R., Hud, N.V.

J. Biomol. Struc. Dynam. 31 suppl., 12, **2013**; doi: 10.1080/07391102.2013.786442

Variable temperature size exclusion chromatography for the study of the structural changes in G-quadruplex

Benabou, S., Eritja, R., Gargallo, R.

ISRN Biochemistry 2013, article ID 631875, 7 pages **2013**; doi: 10.1155/2013/631875

Publications
(books and book chapters)

Electrochemical characterization of guanine quadruplexes

Chiorcea-Paquim, A.M., Santos, P., Diculescu, V.C., Eritja, R., Oliveira-Brett, A.M.

in *Guanine quartets – structure and application*, (Spindler, L., Fritzsche W. Eds), RSC Ed., London, pp 100-109 (2013).

doi: 10.1039/9781849736954-0100

Synthesis and properties of oligonucleotides forming G-quadruplexes

Aviñó, A, Eritja, R.

in *Guanine quartets – structure and application*, (Spindler, L., Fritzsche W. Eds), RSC Ed., London, pp 89-99 (2013).

doi: 10.1039/9781849736954-0089

Functionalization of surfaces with synthetic oligonucleotides

Manning, B., Eritja, R.

in *Methods in Molecular Biology*, Vol. 811, 89-100 (2012). *Nanotechnology Regenerative Medicine: Methods and Protocols*. (J.A. Planell, M. Navarro Eds.) Humana Press, Springer, New York, doi: 10.1007/978-1-61779-388-2_6.

Research projects

Multifuncional nanotechnology for selective detection and treatment of cancer (MULTIFUN)

CCEE, FP-7-NMP-LA-2011-262943
2011-2015

Estudios estructurales de biomoleculas de interés biomédico y tecnológico

MINECO, CTQ2010-20541-C03-01
2011-2013

Multi-scale formation of functional nanocrystal-molecule assemblies and architectures (FUNMOL)

CCEE NMP-2007-213382,
2008-2012

Desarrollo de biosensores para la detección de la fibrosis cística basados en biomembranas híbridas.

Secretaria de Estado de cooperación internacional.
(AECID A1/038984/11)
2012.

Soluciones innovadoras para acelerar la identificación y desarrollo de fármacos para patologías del sistema nervioso.

CDTI (DENDRIA-CEN-20101923)
2011-2013

Research highlights

Control of the gene expression inhibitory properties of nucleic acids by chemical modification.

The use of synthetic oligonucleotides to control gene expression has triggered the search for new oligonucleotide derivatives with improved therapeutic potential. In these cases nucleic acids are used for the inhibition of a specific gene by blocking gene translation or gene transcription or by stimulating the degradation of a particular messenger RNA. Different strategies are possible. In the antisense strategy synthetic oligonucleotides complementary to the messenger RNA of a given gene are used to inhibit translation of messenger RNA to protein. In the siRNA strategy, small RNA duplexes complementary to messenger RNA bind to a protein complex named RISC. siRNA duplexes contains two strands: the antisense or guide strand that binds to RISC and the sense or passenger strand that is released as a result of the interaction of the siRNA duplex with

RISC. The complex formed by the antisense or guide RNA strand and the protein complex RISC is able to catalyze the efficient degradation of a specific messenger RNA, lowering the amount of target protein.

During these years we have concentrated our efforts in the development of novel derivatives of RNA to enhance RNA interference. The results achieved by the group are summarized below.

1. ***Stability of siRNA in serum***. In a recent study, we prepared a new class of modification aimed at increasing the stability of oligonucleotides against 3'-exonuclease degradation (the predominant nuclease activity present in serum) without affecting biological action. Rational design showed the possibility of blocking the hydrolytic activity of 3'-exonucleases by creating a new nucleotide scaffold characterized by its lack of phosphodiester bond linking the two 3'-terminal nucleotide building blocks. Our approach was based on the replacement of the two 3'-terminal nucleotides of an oligonucleotide strand (linked through a 3'-5' phosphodiester bond) by two nucleotide units linked together by an ethyl chain through the exocyclic amino group of the nucleobase. The resulting dimeric nucleoside [N4-ethyl-N4 2'-deoxy-5-methylcytidine derivative (BC)] was connected to the oligonucleotide through a normal phosphodiester bond. Molecular dynamics simulations of a 3'-BC-modified DNA: 3'-exonuclease (Klenow Fragment of E. coli DNA polymerase I) complex suggested that this kind of modification had negative effects on the correct positioning of the adjacent phosphodiester bond at the active site of the enzyme, due to steric clashes between the alkyl linker and amino acid residues (Leu361). We verified that functionalization of the 3'-ends of DNA and RNA strands with BC modifications completely blocked the hydrolytic activity of 3'-exonucleases (KF and snake venom phosphodiesterase). Interestingly, the N-ethyl-N modification confers higher 3'-exonuclease resistance than phosphorothioate bonds. Furthermore, RNA interference experiments with BC-modified siRNAs tar-geting a luciferase gene and an antiapoptotic gene demonstrated that this modification was accepted by the RNAi machinery.

2. ***Cellular uptake***. To address the problem of cellular uptake several siRNA conjugates carrying peptides, lipids, intercalating agents, and carbohydrates were prepared. The best results out of this study were obtained with oligonucleotides carrying lipids and in particular the use of a glycerol derivative functionalized with two linear C14 hydrocarbonated chains. These DNA-lipid conjugates were able to enter the cells without the use of transfecting reagents. In order to rationalize this result we started collaboration with Dr. Alkorta and Dr. Goñi (UPV) for the study of the interaction between 5'-lipid-C28-DNA with the cell membrane using different cell lines and model membrane systems. This double-tail lipid modification showed better incorporation into both lipid model membranes and cell systems. Indeed, this lipid conjugation was capable of inserting the oligonucleotides into both liquid-disordered and liquid-ordered domains of model lipid bilayer systems and produced an enhancement of oligonucleotide uptake in cells, even better than the effect caused by lipoplexes. In addition, in β2 integrin (CR3) expressing cells this receptor was directly involved in the enhanced internalization of this compound.

DNA origami, G-quadruplex and DNA repair..

A remarkable development in the DNA nanotechnology field was been the development of DNA origami by Paul Rothemund, where a long scaffold strand is folded with the help of hundreds of short 'staples' to create the desired two-dimensional shape. In a recent publication DNA origami has been used to visualize the effect of the structure of DNA aptamer binding to thrombin. A series of aptamers that have a quadruplex structure that provides affinity to thrombin were arranged on the right side of a flat DNA origami structure. The same sequences with a modification that prevents the formation of the quadruplex were placed on the left side. By atomic force microscopy (AFM) we could visualize that thrombin only binds to the site with sequences that can fold in the adequate quadruplex structure. Chemical modification introduced in the left origami can be repair by an enzyme involved in the resistance of cancer cells to chemotherapy. This system allows also the visualization by AFM of the repair activity of this DNA repair enzyme involved in cancer.

G-quadruplex and i-motif.

Guanine-rich sequences capable of forming G-quadruplex structures have been found in telomeres and in transcriptional regulatory regions of important oncogenes, such as c-myc, and c-kit. Ligands that selectively bind and stabilize these structures have become appealing anticancer drugs. We have started a study of G-quadruplex structures present at the initiation sites of oncogenes, as well as a study of their interaction with small drugs. Moreover, we studied the interaction of G-rich sequences with their complementary C-rich strands that may also form a quadruplex structure known as i-motif. This work has been done in collaboration with the group of Raimundo Gargallo (UB). A detailed analysis of the equilibrium formed by the G-quadruplex of TBA and oncogenes such and the corresponding complementary C-rich sequences was carried out in order to determine the relative amount of duplex or quadruplexes at different pHs.

Design of inhibitors of DNA repair mechanism in cancer chemotherapy.

Chemotherapy still constitutes the major pharmacological approach against cancer. Antiproliferative drugs are highly cytotoxic and aggressive agents. Under attack, the biochemical repair systems of the cancer cell machinery respond, trying to mitigate the cellular damage induced by these agents. As a result, their clinical efficacy is often limited. High doses are required and as a consequence serious secondary effects are commonplace. Recent advances in the molecular biology of cancer have identified key pathways involved in the DNA repair pathways induced by chemotherapeutic agents. As methylating agents are concerned, two main mechanisms have been envisaged. One involves the O6-methylguanine-DNA-methyltransferase (hAGT), which removes the methyl/alkyl group from the O6 position of guanine. A second important mechanism is the base excision repair (BER) pathway, which is involved in the repair of adducts resulting from methylation of the N7 position of guanine (N7-mG)s. The objective of this project is the development of potent inhibitors of hAGT and APE1, a key endonuclease in the BER pathway. To this end, a combination of X-ray crystallography and in silico virtual screening of chemical libraries is being used. Recently, the first Ape 1 inhibitors have been identified. Some of the compounds identified inhibitors through a docking-based virtual screening technique have in vitro activities in the low-to-medium micromolar range. Interaction of these compounds with the Ape1 protein was observed by mass spectrometry. These molecules also potentiate the cytotoxicity of the chemotherapeutic agent methyl methanesulfonate in fibrosarcoma cells. This study demonstrates the power of docking and virtual screening techniques as initial steps in the design of new drugs, and opens the door to the development of a new generation of Ape1 inhibitors. This research line of the group is supervised by Dr. Carme Fàbrega.

Colloid and Interfacial Chemistry

The main objectives of the group are the study of surfactant self-aggregation processes to contribute in the development of nanotechnological applications. The knowledge on basic aspects of surfactant aggregates (micelles, liquid crystals, vesicles) and colloidal dispersions (microemulsions, nano-emulsions, etc.) allows their use as nanoreactors for the preparation of novel nanostructured materials and as controlled drug delivery systems.

STAFF

CONXITA SOLANS MARSÀ, GROUP LEADER
NURIA AZEMAR SAZATORNIL

TECHNICIAN

AMALIA VÍLCHEZ FERNÁNDEZ

Ph. D.

GABRIELA CALDERÓ LINNHOFF
SHEILA CONTANT
AURORA DOLS
JEREMIE NESTOR
ALESSANDRO PATTI

Ph. D. STUDENTS

JOSÉ JAVIER BURGOS MÁRMOL
CRISTINA FORNAGUERA
MARÍA HOMS SAN MILLÁN
STEFANIE LEITNER
MARIA DEL CARMEN LENDÍNEZ GRIS
MERITXELL LLINÀS PONS
RODRIGO MAGAÑA RODRIGUEZ
JORDI NOLLA ANGUERA
CAMILLE PAULME
KELLY LIDIA PEMARTIN
NEUS VILANOVA GARCÍA

Publications (articles)

Design of biocompatible surface-modified polyurethane and polyurea nanoparticles.

Morral-Ruíz G, Melgar-Lesmes P, García ML, Solans C, García-Celma MJ

Polymer, 53, 6072-6080, 2012

Nano-emulsiones: formación mediante métodos de baja energía e interés en formulaciones cosméticas.

Solé I, Solans C,

NCP-Noticias de Cosmética y Perfumería 328, 5-12, 2012

Nano-emulsions: Formation by low-energy methods.

Solans C, Solé I,

Curr. Op. Colloid & Interface Science, 17, 246–254, 2012

Diffusion in highly concentrated emulsions.

Calderó G, Patti A, Llinàs M, García-Celma MJ,

Curr. Op. Colloid & Interface Sci., 17, 255–260, 2012

Brownian dynamics and dynamic Monte Carlo simulations of isotropic and liquid crystal phases of anisotropic colloidal particles: A comparative study.

Patti A, Cuetos A,

Physical Review E 86, 011403, 2012

In situ Raman and time-resolved luminescence investigation of the local structure of ZrO2 in the Amorphous to Crystalline Phase Transition.

Tiseanu C, Parvulescu VI, Cojocaru B, Pemartin K, Sanchez-Dominguez M, Boutonnet M.

J. Phys. Chem. C, 116, 16776-16783, 2012

Synthesis of ZnO and ZnO2 nanoparticles by the oil-in-water microemulsion reaction method.

Pemartin K, Solans C, Vidal-Lopez G, Sanchez-Dominguez M.

Chem. Lett., 41(10), 1032-1034, 2012.

Frustration of the isotropic-columnar phase transition of colloidal hard platelets by a transient cubatic phase.

Marechal M, Patti A, Dennison M, Dijkstra M.

Phys. Rev. Lett., 108, 206101, 2012.

Comparison and functionalization study of micro-emulsion-prepared magnetic iron oxide nanoparticles.

Okoli C, Sanchez-Dominguez M, Boutonnet M, Järås S, Civera C, Solans C, Kuttuva GR.

Langmuir, 28, 8479-8485, 2012.

Effect of salts on the phase behavior and the stability of nano-emulsions with rapeseed oil and an extended surfactant.

Klaus A, Tiddy GJT, Solans C, Harrar A, Touraud D, Kunz W.

Langmuir, 28, 8318-8328, 2012.

Study of nano-emulsion formation by dilution of microemulsions.

Solè I, Solans C, Maestro A, González C, Gutiérrez, JM.

J. Colloid Interface Sci., 376, 133–139, 2012.

Formation of pegylated polyurethane and lysine-coated polyurea nanoparticles obtained from O/W nano-emulsions.

Morral-Ruíz G, Solans C, García ML, García-Celma MJ.

Langmuir, 28, 6256–6264, 2012.

Preparation of meso/macroporous materials in highly concentrated emulsions based on cubic phases by a single-step method.

Esquena J, Nestor J, Vílchez A, Aramaki K, Solans C.

Langmuir, 28 (33), 12334–12340, 2012.

Solvent-free model for self-assembling amphiphilic cyclodextrins. An off-lattice Monte Carlo approach in two dimensions.

Patti A, Ramsch R, Solans C.

J. Phys. Chem. B, 116, 2687-2695, 2012.

Two-photon confocal imaging study: Cell uptake of two photon dyes-labeled PAMAM dendrons in HeLa cells.

Tsai H-C, Imae T, Calderó G, Solans C.

J Biomed Mater Res Part A, 100A, 746–756, 2012.

Macrocyclic ionic liquid crystals.

Casal-Dujat L, Penon O, Rodríguez-Abreu C, Solans C, Pérez-García L.

New J. Chem., 36, 558–561, 2012.

Physicochemical Characterization of Natural-Like Branched-Chain Glycosides towards Formation of Hexosomes and Vesicles

Noraini Ahmad, Roland Ramsch, Jordi Esquena, Conxita Solans, Hairul Anuar Tajuddin and Rauzah Hashim

Langmuir, 28 (5), 2395–2403, 2012.

Oil-in-Alcohol Highly Concentrated Emulsions as Templates for the Preparation of Macroporous Materials

Susana Vílchez, Lourdes A. Pérez-Carrillo, Jonathan Miras, Conxita Solans, and Jordi Esquena

Langmuir, 28 (20), 7614–7621, 2012.

Emulsions and microemulsions

K. Aramaki, C. Solans

Editorial overview. Curr Opin Colloid In, 17 (5), 233-234, 2012.

Preparation of novel silicone multicompartment particles by multiple emulsion templating and their use as encapsulating systems.

Vilanova N, Solans C, Rodríguez-Abreu C.

Langmuir, 29 (49), 15414–15422, 2013.

Nanocarriers from dicationic bis-imidazolium amphiphiles and their interaction with anionic drugs.

Casal-Dujat L, Griffiths PC, Rodríguez-Abreu C, Solans C, Rogers S, Pérez-García L.

J. Mater. Chem. B, 1, 4963-4971, 2013.

Chitosan macroporous foams obtained in highly concentrated emulsions as templates.

Miras J, Vílchez S, Solans C, Esquena J.

J. Colloid Interface Sci., 410, 33–42, 2013.

Conductive microemulsions for template CoNi electrodeposition.

Serrà A, Gómez E, Calderó G, Esquena J, Solans C, Vallés E.

Phys. Chem. Chem. Phys., 15, 14653-14659, 2013.

Multifunctional polyurethane–urea nanoparticles to target and arrest inflamed vascular environment: A potential tool for cancer therapy and diagnosis.

Morral-Ruíz G, Melgar-Lesmes P, Solans C, García-Celma MJ.

J. Controlled Release, 171, 163–171, 2013

Polymerization of hexyl methacrylate in nanoemulsions made by low and high energy methods.

Alvarado AG, Pérez-Carrillo LA, Arellano M, Rabelero M, Ceja I, Mendizábal, E, Solans C, Esquena J, Puig JE

J. Macromol. Sci., Part A: Pure and Applied Chemistry, 2013, 50, 812–820, 2013.

Electrostatic binding and hydrophobic collapse of peptide–nucleic acid aggregates quantified using force spectroscopy.

Camunas-Soler J, Frutos S, Bizarro CV, de Lorenzo S, Fuentes-Perez ME, Ramsch R, Vilchez S, Solans C, Moreno-Herrero F, Albericio F, Eritja R, Giralt E, Dev SB, Ritort F.

ACS Nano, 7 (6), 5102–5113, 2013.

Fabrication of novel silicone capsules with tunable mechanical properties by microfluidic techniques.

Vilanova N, Rodríguez-Abreu C, Fernández-Nieves A, Solans C.

ACS Appl. Mater. Interfaces, 5 (11), 5247–5252, 2013.

Preparation, characterization, and release properties of hydrogels based on hyaluronan for pharmaceutical and biomedical use.

Roig-Roig F, Solans C, Esquena J, García-Celma MJ.

J. Appl. Polym. Sci., 1377-1382, 2013.

Surface functionalization of macroporous polymeric materials by treatment with air low temperature plasma.

Molina R, Sole I, Vílchez A, Bertran E, Solans C, Esquena J.

J. Nanosci. Nanotech., 13(4), 2819-2825, 2013.

Poly(hexyl methacrylate) nanoparticles templating in nanoemulsions-made by phase inversion temperature.

Alvarado AG, Nolla J, Rabelero M, Pérez-Carrillo LA, Arellano M, Mendizábal E, Solans C, Puig JE,

J. Macromol. Sci., Part A: Pure and Applied Chemistry, 50(4), 385-391, 2013.

Microemulsions as reaction media for the synthesis of mixed oxide nanoparticles: relationships between microemulsion structure, reactivity, and nanoparticle characteristics.

Aubery C, Solans C, Prevost S, Gradzielski M, Sanchez-Dominguez M.

Langmuir, 29, 1779-1789, 2013.

Effects of the functionalizing agent, itaconic acid, on the mechanical properties of microemulsion-made core/shell polymers.

Rabelero M, Trujillo A, Ceja I, Canché G, Mendizábal E, Esquena J, Solans C, Puig JE

Polym. Eng. Sci., 53(7), 1529–1535, 2013.

Facile synthesis of meso/macroporous dual materials with ordered mesopores using highly concentrated emulsions based on a cubic liquid crystal.

Nestor J, Vílchez A, Solans C, Esquena J.

Langmuir, 29 (1), 432–440, 2013.

Facile synthesis of dual micro/macroporous carbonaceous foams by templating in highly concentrated water-in-oil emulsions.

Alam MM; Miras J, Perez-Carrillo LA, Vilchez S, Solans C, Imae T, Ujihara M, Esquena, J. Microporous Mesoporous Mat., 182, 102-108, 2013.

New insights on the mechanisms of drug release from highly concentrated emulsions.

Llinàs M, Calderó G, García-Celma MJ, Patti A, Solans C,

J Colloid Interface Sci, 394, 337–345, 2013.

Validation of methods for the detection and quantification of engineered nanoparticles in food.

Linsinger, TPJ, Chaudhry Q, Dehalu V, Delahaut P, Dudkiewicz A, Grombe R, Von Der Kammer F, Larsen EH, Legros S, Loeschner K, Peters R, Ramsch R, Roebben G, Tiede K, Weigel S.

Food Chemistry, 138, 1959–1966, 2013.

Modeling the aggregation behavior of amphiphiles in the continuous phase of highly concentrated emulsions.

Patti A.

Colloids and Surfaces A: Physicochem. Eng. Aspects, 437, 90– 100, 2013.

Microemulsions for obtaining nanostructures by means of electrodeposition method

Serrá A, Gómez E, Calderó G, Esquena J, Solans C, Vallés E,

Electrochem. Comm., 27, 14–18, 2013

Kinetics of chitosan hydrogel formation in high internal phase oil-in-water emulsions (HIPEs) using viscoelastic measurements

Jonathan Miras, Susana Vílchez, Conxita Solans, Tharwat Tadros, Jordi Esquena

Soft Matter, 9 (36), 8678-8686, 2013.

Publications
(books and book chapters)

Preparation, stability and applications of nano-emulsions.

Solans C, Solè I, Lozsan A,

Topics in the Colloidal Aggregation and Interfacial Phenomena (Ed. Garcia-Sucre M,. Loszan A, Castellanos-Suarez AJ, Toro-Mendoza J). Research Signpost. Kerala, India, pp. 1-25, 2012.

Formation of nanoemulsions by low-energy methods and their use as templates for the preparation of polymeric nanoparticles.

Calderó G, Solans C,

Handbook of Green Chemistry. Volume 8: Green Nanoscience. (Ed. Anastas, P.T.). Wiley-VCH, Weinheim, Germany, pp. 165-174, 2012.

New trends on the synthesis of inorganic nanoparticles using microemulsions as confined reaction media.

Sanchez-Dominguez M, Aubery C, Solans C.

Smart Nanoparticles Technology. (Ed. Abbass Hashim), 576 pages, InTech Pub., pp. 195-220, 2012.

Oil-in-water microemulsions for the synthesis of nanocrystalline, mesoporous, and ultrafine CeO2 powders.

Sanchez-Dominguez M, Pemartin K, Solans C, Boutonnet M

Colloid and Interface Chemistry for Nanotechnology. (Ed. Kralchevsky P, Miller R, Ravera F) CRC Press Inc., pp. 177-198, 2013.

Polymeric O/W nano-emulsions obtained by the phase inversion composition (PIC) method for biomedical nanoparticle preparation.

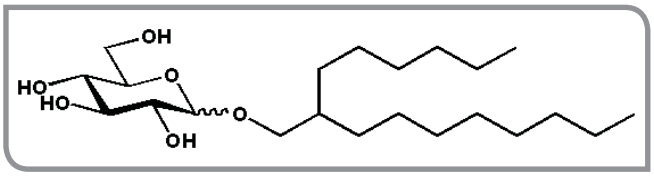
Calderó G, Solans, C.

Emulsion Formation and Stability. (Ed. Tadros TF), Wiley-VCH, Weinheim, Germany, pp199-207, 2013

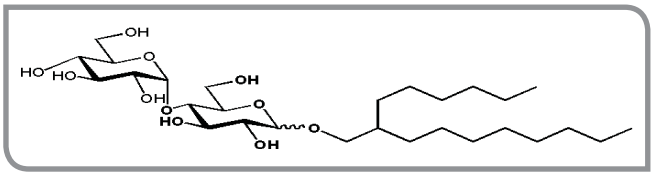
Research highlights

Amphiphile Self-assembly

Self-assembly studies of amphiphilic molecules are conducted in the group as a bottom up approach for the development of well-defined nanostructures in view of their use as nanocarriers (e.g. controlled drug delivery systems), nanoreactors (e.g. synthesis of advanced materials), tailor-made formulations, etc. During this period, the self-organizing structures formed by two synthetic branched-chain glycolipids (Figure 1) have been studied by determining the phase behavior under thermotropic and lyotropic conditions (N. Ahmad, Langmuir, 2012).



Glucoside derivative



Maltoside derivative

Figure 1. Chemical structures of (2-hexyldecylb(/a)--D-glucoside (2-HDG) and (B) 2-hexyldecyl-b(/a)-D-maltoside.

The thermotropic study showed that the glucoside derivative formed a columnar hexagonal liquid crystalline phase, whereas in aqueous media, it formed inverted hexagonal liquid crystalline phase in equilibrium with excess aqueous solution, i.e. hexosome dispersion (Figure2).

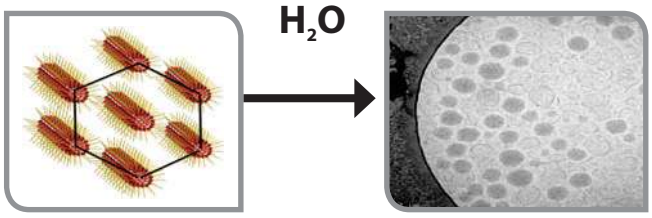


Figure 2. Schematic representation of an hexagonal liquid structure and Cryo-TEM micrograph of ahexosome dispersion with 0.50 wt% of the glucoside derivate (shown in Figure 1) in water.

It was also shown that the maltoside derivative (Figure 1), as a surfactant with more balanced hydrophilic-lipophilic properties than the glucoside derivate, forms lamellar liquid crystalline phases in aqueous solution leading to the formation of multilamellar vesicles (MLV).

Emulsions: Formation by Low-energy Methods and Properties

Emulsification by low-energy methods produce, generally, emulsions with smaller and more uniform droplets. New knowledge on low-energy emulsification methods has been acquired by studying the effect of different dilution procedures on the formation of nano-emulsions obtained by dilution of W/O and O/W microemulsions (I. Solè, J Colloid Interface Sci., 2012). By studying this effect it was clearly shown that dilution of W/O microemulsions only results in nano-emulsions when water is added stepwise and that the same small-size nano-emulsions can be obtained starting emulsification from both W/O and O/W microemulsions.

In the context of emulsion systems, the release of a hydrophilic drug was studied from highly concentrated W/O emulsions at pH values of the dispersed phase ranging between 2 and 12 (M. Llinàs, J Colloid Interface Sci., 2013). Although the release from aqueous solutions was not influenced by pH, the release from HIPREs depended strongly on the pH of the dispersed phase. Increasing the solubility of the drug in the dispersed phase, its apparent diffusion coefficient decreased over two orders of magnitude. Two different physico-chemical models were applied to describe diffusion, showing an excellent agreement with experiments and confirming the role of the structure of the emulsions and the solubility of the drug. It was shown that solubility of the diffusing molecule can have a higher effect on release from HIPREs than the interfacial film properties. The mechanism of release of TP from this type of emulsions was described by three different but simultaneous diffusion steps (Figure 3): 1) Diffusion across the dialysis membrane to the receptor solution; 2) Diffusion through the oil phase of the emulsion and 3) Diffusion across the droplet interfacial film.

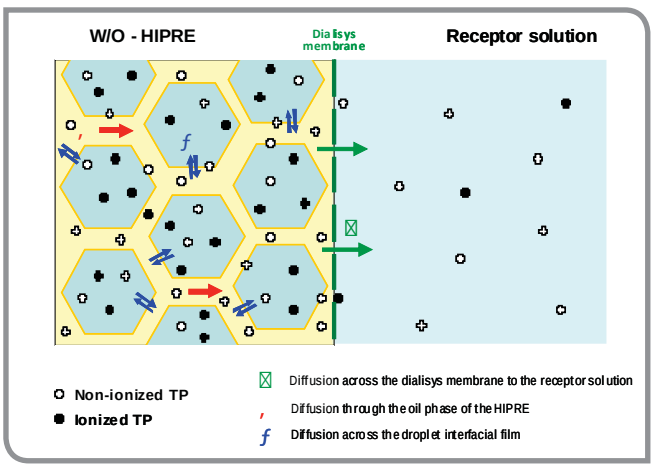


Figure 3. Schematic illustration of the diffusion steps of a hydrophilic drug (TP) from W/O highly concentrated emulsions..

The Microemulsion Reaction Method

Among wet chemistry methods for the synthesis of inorganic nanoparticles, the Microemulsion Reaction Method (MRM) has been found to be a suitable option in order to control size and shape in mild reaction conditions. In this context, phase behavior, dynamics, and structure of w/o microemulsions of the system Aqueous solution / Synperonic® 13_6.5/ 1Hexanol / Isooctane were studied, with the goal of determining their effect on Mn-Zn ferrite nanoparticle formation kinetics and characteristics (C. Aubery, Langmuir, 2013). Microemulsion structure and dynamics were studied systematically by conductivity, Dynamic Light Scattering (DLS), Differential Scanning Calorimetry (DSC) and Small-Angle Neutron Scattering (SANS). The main effect of cosurfactant 1-hexanol was a decrease in microemulsion regions as compared to the systems without cosurfactant. SANS characterization indicated small prolate ellipsoidal micelles.

The main difference regarding the characteristics of the obtained nanoparticles (Figure 4) was observed when bicontinuous microemulsions were used as reaction media which resulted in 8 nm nanoparticles, versus a constant size of ~ 4 nm obtained with all other microemulsions regardless of aqueous solution content, dynamics, and presence or absence of cosurfactant.

A novel approach based on the use of O/W instead of W/O microemulsions for the synthesis of inorganic nanoparticles was developed in the group since our first report on the subject in 2009. The synthesis of, among others, ZnO and ZnO_2 nanoparticles with controlled size was achieved using this method (K. Pemartin, Chem. Lett., 2012). In addition, conductive microemulsions have been developed (A. Serra, Phys. Chem. Chem. Phys., 2013) and used as templates for CoNi electrodeposition. An influence of microemulsion structure on the resulting nanostructures was found.

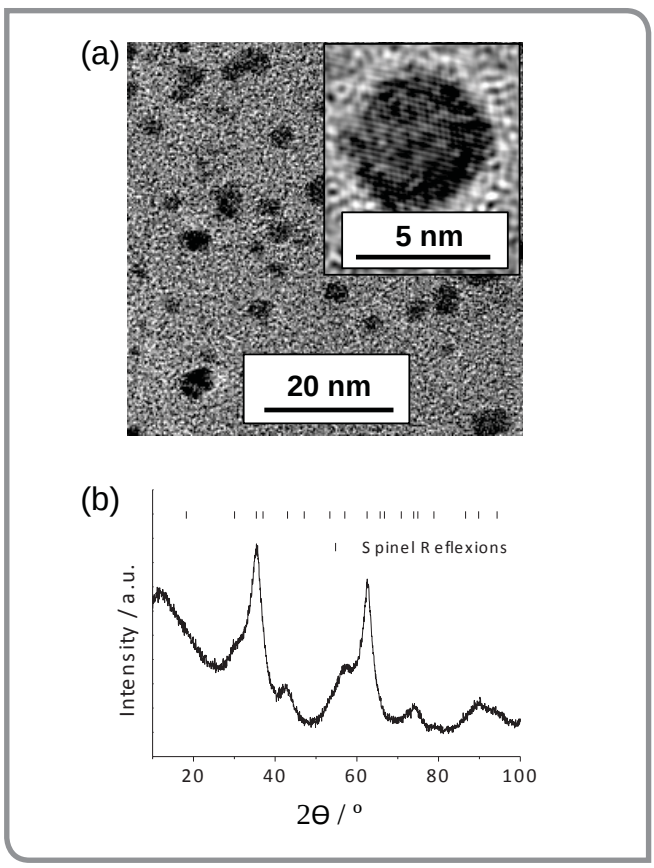


Figure 4 (a) TEM image and (b) XRD pattern of nanoparticles synthesized with the Aqueous solution / Synperonic 13_6.5 : 1-hexanol / Isooctane system at T = 50°C. S:O ratio 20:80, pH = 12.8. Aqueous solution content: 12.5 wt%. Inset in (a) shows High-Resolution TEM (HRTEM).

Cell Therapy

The Cell Therapy group is interested in two related applied-research fields: regenerative medicine and tumor therapy. In the first case, the objective is the analysis of cell behavior in biomaterials used as scaffolds for tissue repair. In the second case, the objective is to develop antitumor therapies using stem cells as vehicles for the local delivery of therapeutic agents and the study of therapeutic-cell tumor interactions. However, both, the procedures and models developed also allow more general analysis of tumor response to chemical and biological agents.

For these studies the group uses mesenchymal stromal cells from adipose tissue. This special stem cell type capable of producing multiple chemokines and growth factors is a very promising therapy agent, not only due to its elevated capacity for multi-lineage differentiation (tissue repair applications) and tumor homing (therapy), but also for its abundance and easy generation from human adipose tissue.

The need to observe the behavior of cells in live animals has led to the development and use of bioluminescence imaging procedures based in the modification of cells with luciferase-gene reporters. Bioluminescence reporters allow the detection and monitoring of cells implanted in live animals, using high sensibility video cameras capable of lineal response ranging six orders of magnitude. In this manner, in spite of the diffusion and absorption of photons by animal tissues, these instruments allow imaging the distribution and proliferation of small populations of bioluminescent cells implanted in live animals. The use of inducible tissue-specific promoters to regulate the expression of luciferase reporters also allows the evaluation of their level of activity and therefore the analysis of changes in gene expression in vivo. Moreover, due to the existence of luciferases that use non cross-reacting substrates, it is possible to monitor two cell populations en the same animal or the expression level of two different reporters in the same cell.

STAFF

JERONIMO BLANCO FERNANDEZ, GROUP LEADER
NURIA RUBIO VIDAL, SENIOR SCIENTIST

Ph.D.

MARTA GUERRA REBOLLO
CRISTINA GARRIDO LOPEZ
SARA RAMOS ROMERO
OLAIA FERNANDEZ VILA

Publications (articles)

Bioluminescence imaging of cardiomyogenic and vascular differentiation of cardiac and subcutaneous adipose tissue-derived progenitor cells in fibrin patches in a myocardium infarct model.

Bagó JR, Soler-Botija C, Casaní L, Aguilar E, Alieva M, Rubio N, Bayes-Genis A, Blanco J.

Int J Cardiol., 169(4):288-95, 2013

In vitro characterization of the molecular machinery regulating umbilical cord blood mesenchymal stem cell angiogenesis: A step towards multipotent stem cell therapy for vascular regeneration.

Roura S, Bagó JR, Gálvez-Montón C, Blanco J, .

J Stem Cell Res Ther, 3, 140, 2013

Endothelial differentiation of adipose tissue-derived mesenchymal stromal cells in glioma tumors: Implications for cell-based therapy.

Bagó JR, Alieva M, Soler C, Rubio N, Blanco J., Bayes-Genis A.

Mol. Ther., 21(9), 1758-66, 2013.

In vivo bioluminescence imaging of cell differentiation in biomaterials: A platform for scaffold development.

Bagó JR, Aguilar E, Alieva M, Soler-Botija C, Vila OF, Claros S, Andrades JA, Becerra J, Rubio N, Blanco J.

Tissue Engineering Part A, 19(5-6): 593-603, 2013.

Calcium phosphate glass improves angiogenesis capacity of poly(lactic acid) scaffolds and stimulates differentiation of adipose tissue-derived mesenchymal stromal cells to the endothelial lineage.

Vila OF, Bagó JR, Navarro M, Alieva M, Aguilar E, Engel E, Planell J, Rubio N, Blanco J,

J Biomed Mater Res A., 101(4), 932-41, 2013.

Peroxiredoxin 2 specifically regulates the oxidative and metabolic stress response of human metastatic breast cancer cells in lungs.

Stresing V, Baltziskueta E, Rubio N, Blanco J, Arriba MC, Valls J, Janier M, Clézardin P, Sanz-Pamplona R, Nieva C, Marro M, Petrov D, Sierra A,

Oncogene, 32(6), 724-35, 2013.

Acid ceramidase as a therapeutic target in metastatic prostate cancer.

Camacho L, Meca-Cortés O, Abad JL, García S, Rubio N, Díaz A, Celià-Terrassa T, Cingolani F, Bermudo R, Fernández PL, Blanco J, Delgado A, Casas J, Fabriàs G, Thomson TM.

J. Lipid Res., 54(5), 1207-20, 2013.

Publications
(books and book chapters)

Research Projects

Red de terapia celular – Tercel

Nacional, RD12/0019/0004

01/01/2013-31/12/2014

Terapia combinada basada dos tipos celulares y dos sistemas de activación de fármacos dirigida al nicho vascular de las células madre de glioblastoma

Nacional, SAF2012-33404

01/01/2013-31/12/2015

Terapia fotodinámica contra el sistema vascular tumoral

Nacional, PRI-PIBIN-2011-1011

01/12/2011-01/12/2014

Desarrollo de un doble agente para terapia celular y para contraste por mri de las celulas vehiculo utilizadas

Nacional, SAF2009-07315-E

01/03/2010-28/02/2013

Desarrollo racional de estrategias de terapia celular antitumoral

Nacional, SAF2009-07102 01/01/2010-30/06/2014

Angiogenesis-inducing Bioactive and Bioresponsive Scaffolds in Tissue Engineering

EECC, 214402

01/12/2008-30/11/2012

Estudio del comportamiento de biomateriales en la generación de tejidos

27/02/2013-26/02/2015

Apoyo tecnológico sobre la regeneración tisular de biomateriales

25/02/2013- 24/05/2013

Convenio entre el CSIC y el centro de investigacion biomedica en red de bioingenieria, biomateriales y nanomedicina - CIBER-BBN - para desarrollar las relaciones entre el CIBER-BBN y el CSIC

Principal Investigators: R. Eritja, C. Solans, M.P. Marco, J. Blanco

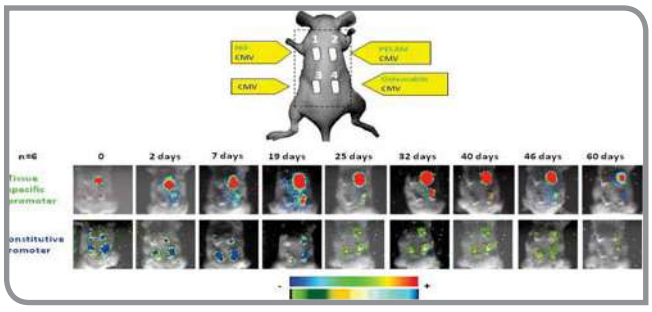
2010-2015

Research Highlights

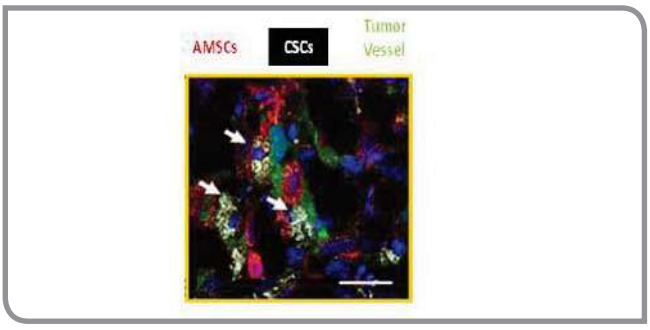
The Cell Therapy group has focused its research activity during recent years in two interrelated aspects of cell therapy: Regenerative Medicine and Tumor Therapy, as well as in the understanding of the interactions between tumor and therapeutic stem cells.

Research highlights during year 2013 have been:

1- Validation and subsequent application of the Biomaterial Analysis Platform, resulting in publications in Tissue Engineering, International Journal of Cardiology and J. Biomed. Mater. Res. (regenerative medicine field). The platform, based in the use of bioluminescence and fluorescence imaging in live animals, allows real time monitoring of cell behavior in biomaterials. For this purpose, cells are labeled with two lentiviral vectors for the expression of chimerical bioluminescent-fluorescent reporters; one for the expression of Photinus pyralis luciferase-green fluorescent protein (PLuc-GFP), regulated by an inducible tissue specific promoter and a second one, for the expression of the chimerical reporter Renilla reniformis luciferase-red fluorescent protein (RLuc-RFP), regulated by a constitutively active promoter. Since photons in images are quantifiable, changes in the ratio PLuc/RLuc are a measure of inducible-promoter activity and can be used as an indicator of differentiation to a specific cell lineage.



2- Demonstration that differentiation of therapy-delivering mesenchymal stem cells to the endothelial lineage and their association with the tumor stem cell niche are required for effective tumor cell killing (tumor therapy field).



3- Participation in several collaborative projects requiring bioluminescence imaging to noninvasively evaluate tumor growth, with results published in Oncogene and Journal of Lipid Research, among other journals.

Surface Chemistry

The main objective is to study the formation and characterization of structured materials, and their applications in novel technological processes. This includes: a) Surface modification of materials by chemical and physical (plasma) methods, b) Surface characterization of textile and polymeric materials, c) Formation and characterization of hydrogels, d) Development of stimuli-responsive textiles by incorporation of advanced nanostructured materials, and e) Preparation and characterization of organic and inorganic porous materials.

STAFF

JORDI ESQUENA MORET, GROUP LEADER
RICARDO MOLINA MANSILLA

TECHNICIAN

MONTSERRAT SINDREU GRAÑE

Ph. D.

CAROLINA AUBERY TORRES
MOHAHMAD MYDUL ALAM
ISABEL SOLÈ FONT
SUSANA VÍLCHEZ MALDONADO

Ph. D. STUDENTS

MARÍA MARTÍNEZ RODRÍGUEZ
JONATHAN MIRAS HERNÁNDEZ
BALTAZAR SILVAN
MANROSHAN SINGH
ALEJANDRO VÍLCHEZ VILLALBA
SILVIA VILCHEZ MALDONADO

POST-GRADUATE STUDENTS

MARÍA ELENA BAUTISTA PÉREZ
LAURA SOBREVIAS

Publications (articles)

Oil-in-alcohol highly concentrated emulsions as templates for the preparation of macroporous materials.

Vílchez S, Pérez-Carrillo LA, Miras J, Solans C, Esquena J.

Langmuir, 28(20), 7614-7621, 2012

Polymerization-induced phase separation as a one-step strategy to self-assemble alkanethiol-stabilized gold nanoparticles inside polystyrene domains dispersed in an epoxy matrix.

Romeo HE, Vílchez A, Esquena J, Hoppe CE, Williams RJ.

Eur. Polymer J., 48(6), 1101-1109, 2012

Microstructured objects produced by the supramolecular hierarchical assembly of an organic free radical gathering hydrophobic-amphiphilic characteristics.

Vera F, Mas-Torrent M, Esquena J, Rovira C, Shen Y, Nakanishi T, Veciana J,

Chem. Sci., 3(6), 1958-1962, 2012

Drug delivery properties of macroporous polystyrene solid foams.

Canal C, Aparicio RM, Vílchez A, Esquena J, García-Celma MJ.

J. Pharm. Pharmaceut. Sci., 15(1), 197-207, 2012

Physicochemical characterization of natural-like branched-chain glycosides towards formation of hexosomes and vesicles.

Ahmad N, Ramsch R, Esquena J, Solans C, Tajuddin HA, Hashim R.

Langmuir, 28(5), 2395–2403, 2012

Preparation of meso/macroporous materials in highly concentrated emulsions based on cubic phases by a single-step method.

Esquena J, Nestor J, Vílchez A, Aramaki K, Solans C.

Langmuir, 28 (33), 12334–12340, 2012.

Dyeing of plasma treated wool with commercially available natural colorants.

Paul R, Erra P, Molina R.

International Dyer 197, 32-35, 2012

Chitosan macroporous foams obtained in highly concentrated emulsions as templates.

Miras J, Vílchez S, Solans C, Esquena J.

J. Colloid Interface Sci., 410, 33–42, 2013.

Conductive microemulsions for template CoNi electrodeposition.

Serrà A, Gómez E, Calderó G, Esquena J, Solans C, Vallés E.

Phys. Chem. Chem. Phys., 15, 14653-14659, 2013.

Polymerization of hexyl methacrylate in nanoemulsions made by low and high energy methods.

Alvarado AG, Pérez-Carrillo LA, Arellano M, Rabelero M, Ceja I, Mendizábal, E, Solans C, Esquena J, Puig JE

J. Macromol. Sci., Part A: Pure and Applied Chemistry, 2013, 50, 812–820, 2013.

Preparation, characterization, and release properties of hydrogels based on hyaluronan for pharmaceutical and biomedical use.

Roig-Roig F, Solans C, Esquena J, García-Celma MJ.

J. Appl. Polym. Sci., 1377, 2013.

Surface functionalization of macroporous polymeric materials by treatment with air low temperature plasma.

Molina R, Sole I, Vílchez A, Bertran E, Solans C, Esquena J.

J. Nanosci. Nanotech., 13(4), 2819-2825, 2013.

Effects of the functionalizing agent, itaconic acid, on the mechanical properties of microemulsion-made core/shell polymers.

Rabelero M, Trujillo A, Ceja I, Canché G, Mendizábal E, Esquena J, Solans C, Puig JE

Polym. Eng. Sci., 53(7), 1529–1535, 2013.

Facile synthesis of meso/macroporous dual materials with ordered mesopores using highly concentrated emulsions based on a cubic liquid crystal.

Nestor J, Vílchez A, Solans C, Esquena J.

Langmuir, 29 (1), 432–440, 2013.

Facile synthesis of dual micro/macroporous carbonaceous foams by templating in highly concentrated water-in-oil emulsions.

Alam MM; Miras J, Perez-Carrillo LA, Vilchez S, Solans C, Imae T, Ujihara M, Esquena, J

Microporous Mesoporous Mat., 182, 102-108, 2013.

Microemulsions for obtaining nanostructures by means of electrodeposition method.

Serrá A, Gómez E, Calderó G, Esquena J, Solans C, Vallés E,

Electrochem. Comm., 27, 14–18, 2013

Robust molecular micro-capsules for encapsulating and releasing hydrophilic contents.

Vera F, Mas-Torrent M, Avci C, Arbiol J, Esquena J, Rovira C, Veciana J.
Chem. Commun., 49, 7827-7829, 2013

TiO2(SiO2)x and ZrO2(SiO2)x cryogels as catalysts for the citronellal cyclization to isopulegol.

Jimeno C, Miras J, Esquena J.
Catalysis Lett., 143(6), 616-623, 2013.

Kinetics of chitosan hydrogel formation in high internal phase oil-in-water emulsions (HIPEs) using viscoelastic measurements

Jonathan Miras, Susana Vílchez, Conxita Solans, Tharwat Tadros, Jordi Esquena
Soft Matter, 9 (36), 8678-8686, 2013.

Electrostatic binding and hydrophobic collapse of peptide–nucleic acid aggregates quantified using force spectroscopy.

Camunas-Soler J, Frutos S, Bizarro CV, de Lorenzo S, Fuentes-Perez ME, Ramsch R, Vilchez S, Solans C, Moreno-Herrero F, Albericio F, Eritja R, Giralt E, Dev SB, Ritort F.

ACS Nano, 7 (6), 5102–5113, 2013.

Aqueous Solutions of NIPAAm Initiated by Atmospheric Plasma Treatment.

Molina R, Ligero C, Jovancic P, Bertran E.

Plasma Processes and Polymers, 10(6), 506–516, 2013.

Parametric Study of CF4-plasma on the Hydrophobicity of Polyester Synthetic Leather.

Kwong CH, Ng S, Kan CW, Molina R.

Fibers and Polymers, 14(10), 1608-1613, 2013.

Removal of cyanide from water by means of plasma discharge technology.

Hijosa-Valsero M, Molina R, Schikora H, Müller M, Bayona JM.

Water Research, 47(4),1701-1707, 2013.

Removal of priority pollutants from water by means of dielectric barrier discharge atmospheric plasma

Hijosa-Valsero M, Molina R, Schikora H, Müller M, Bayona JM.

Journal of Hazardous Materials, 262(15), 664-673, 2013.

Surface plasma treatment to enhance hydrophobicity of textiles

Kwong CH, Ng S,Kan CH, Yuen CWM, Chan CK, Molina R.

Textile Asia, 44(3), 20-23, 2013.

Surface functionalization of macroporous polymeric materials by treatment with air low temperature plasma.

Molina R, Sole I, Vílchez A, Bertran E, Solans C, Esquena J.

J. Nanosci. Nanotech., 13(4), 2819-2825, 2013.

Publications
(books and book chapters)

Formulation, characterization, and property control of paraffin emulsions, in emulsion formation and stability ch6.

Esquena, J, Vilasau J

Emulsion Formation and Stability (Tadros TF. Ed.), Wiley-VCH, Weinheim, Germany, pp. 169-197, 2013.

Low-Density Solid Foams Prepared by Simple Methods Using Highly Concentrated Emulsions as Templates

Jordi Esquena.

Colloid and Interface Chemistry for Nanotechnology (Ed. Kralchevsky P, Miller R, Ravera F) CRC Press Inc., pp. 199, 2013.

Research projects

Nuevos apósitos activos biocompatibles basados en factor tisular recombinante con propiedades hemostáticas / sellantes

Proyecto Innpacto, IPT-2012-0348-010000

2013-2014

Formación de emulsiones de Pickering mediante métodos de baja energía para la preparación de nuevos materiales porosos nanocompuestos

Proyecto del plan Nacional de I+D+i, CTQ2011-23842

2012-2014

Investigación y desarrollo de textiles de uso médico y/o terapéutico mediante procesos de funcionalización superficial (Advanmedtex)

Proyecto Innpacto, IPT-300000-2010-026

2010-2013

Advanced functional organic-inorganic nanocomposites by cooperative self-assembly (NANOITSELF)

Proyecto europeo, 230810

2010-2012

Ayudas para apoyar las actividades de los grupos de investigación. Nombre del grupo: Tensioactius

Generalitat de Catalunya, 2009SGR961
2009-2014

Mezclas bituminosas de altas prestaciones, formuladas con nuevas tecnologías de baja temperatura.

Contrato con empresa
2012-2014

Obtención de emulsiones de simeticona estables

Contrato con empresa
2012-2013

The use of low temperature and low pressure plasma for dry sterilization of the inside parts of reactors

Pierre Fabre S.A.
2011-2014

Research highlights

Gelatin foams as medical biomaterials for wound healing in surgery

Gelatin is a protein obtained by partial hydrolysis of native collagen from skin and bones of animals. It is readily available, with low cost. Due to its biocompatibility and biodegradability, gelatin sponges have been used in medical applications as hemostatic foams, what makes it an effective, quick and easy to use wound dressing/healing material.

Gelatin-based solid foams can absorb blood or body fluids, as well as deliver active pharmaceutical ingredients (API's), which can be antibiotics, accelerating the healing process. Therefore, gelatin foams can be an effective, quick and easy to use wound dressing/healing material.

In the Surface Chemistry Group, gelatin-based sponges have been obtained by different methods of preparation and pore morphology has been controlled, depending on parameters such as gelatin concentration, temperature, gas flow rate, freezing rate/temperature, etc., as showed in Fig. 1.

Also, in order to obtain sponges with desired dissolution rates and mechanical properties, a variety of chemical and physical crosslinking methods have been used. Dissolution rate is related to the period of time the sponge will remain in the body until complete absorption. Mechanical properties such as elongation and tensile strength give us an indication of its behavior during manipulation in surgical operations.

Formulation of emulsions for road pavement

Bitumen formulations have very important applications in road pavement, since bitumen has strong surface adhesion, high internal cohesion and low water permeability. In road constructions, the conventional pavement process consists in mixing the bitumen with gravel and filler particles at temperatures above 120ºC, and the hot slurry is applied on the road. This process has economical and environmentally disadvantages, because of high energy consumption and release of toxic vapors. An alternative process for road construction is the use of bitumen-in-water emulsions, allowing the application at ambient temperature. However, this process usually requires long times for water evaporation, delaying road re-opening. This problem can be solved by using highly concentrated bitumen-in-water emulsions, which contain smaller amounts of water.

In this context, a technological challenge is to obtain highly concentrated bitumen emulsions with small and more uniform droplet size, because of the extremely high viscosity of bitumen. In the present

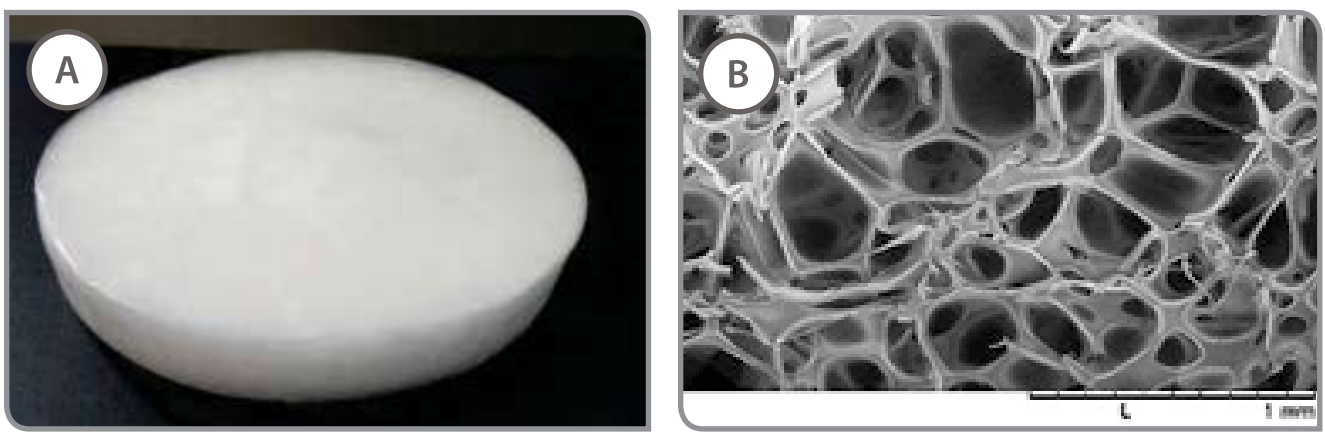


Fig. 1. Examples of a gelatin-based sponge, developed in IQAC-CSIC.
a) visual aspect; b) SEM image.

work, emulsions with small droplet size have been prepared by controlling the viscosity of the emulsion aqueous phase. For this purpose, either chitosan or polyacrylamide were selected as cationic thickeners. The emulsions were obtained by a method consisting in step-wise addition of the bitumen to the aqueous phase [1], which contained surfactant and thickener, at 90ºC. An example is shown in Fig. 2.

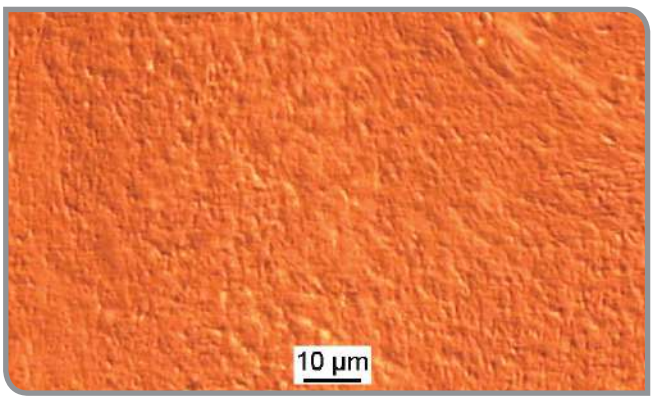


Fig. 2. Image acquired by optical microscopy of a highly concentrated emulsion of bitumen (90 wt%) in water. (Reproduced from Ref. [1]).

The results demonstrated that the droplet size could be decreased by increasing the viscosity of the continuous phase, obtaining bitumen-in-water highly concentrated emulsions with small droplet size. Moreover, the droplet size could be controlled in a rather wide range.

[1] M. Martínez, C. Solans, F. Valor, J. López, E. Tomás, J. Esquena, Proceedings of the World Congress on Emulsions (2010) Lyon, France.

Emulsions stabilized by nanoparticles (Pickering emulsions)

It is well known that solid particles (covering the nano- to micro- range) can adsorb at interfaces and consequently stabilize emulsions. Such emulsions are known in the literature as Pickering emulsions and play an important role in numerous industrial applications. Particles, unlike surfactants, do not (at least significantly) reduce the free energy of a liquid–liquid interface by reducing the interfacial tension; the surface energy can be lowered simply because the area of such interface is reduced when particles are adsorbed.

In the Surface Chemistry Group, highly concentrated Pickering emulsions have been prepared with magnetite (Fe_3O_4) nanoparticles, and a systematic study of the antagonistic interactions between magnetite nanoparticles (Fe_3O_4) and a nonionic hydrophobic surfactant have been carried out.

Stable W/O highly concentrated emulsions can be prepared using partially hydrophobized magnetite nanoparticles. These emulsions experience phase separation when the surfactant is added at concentrations as low as 0.05 wt %. Such phase separation arises from the preferential affinity of the surfactant for the surface of nanoparticles, which remarkably enhances particle hydrophobicity, leading to a gradual desorption of nanoparticles from the interface. W/O emulsions were obtained at higher surfactant concentrations, but in this case, these emulsions are mainly stabilized by surfactant molecules. Therefore, stable emulsions could be prepared in two separate ranges of surfactant concentrations. After polymerization of the external emulsion phase, low-density macroporous polymers were obtained, and the adsorption and aggregation of nanoparticles was analyzed by transmission electron microscopy.

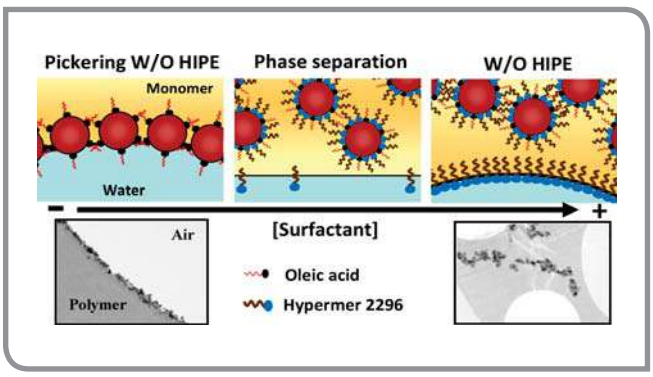


Fig. 3. Scheme showing an example of antagonistic interactions between surfactant and nanoparticles in Pickering emulsions. (Reproduced from Ref. [2])

The progressive displacement of nanoparticles, as a function of surfactant concentration, was revealed: from the oil–water interface, in which nanoparticles were adsorbed forming dense layers, to the continuous phase of the emulsions, where small nanoparticle aggregates were randomly dispersed.

[2] A. Vílchez, C. Rodríguez-Abreu, A. Menner, A. Bismarck, J. Esquena, Langmuir 30 (2014) 5064-5074.

5

Department of Chemical and Surfactants Technology

Department of Chemical and Surfactants Technology

Head: Ramon Pons Pons / Mª Teresa García Ramon

The research in the Department focus on theoretical and applied aspects of product and chemical processes technology with special incidence in the synthesis, the physical chemistry and the biology of surfactants. This research is relevant in the lines of Sustainable Chemistry and Nanotechnology of soft matter and look for environmental and human health improvement. Among the scientific activities, with relation to the Sustainable Chemistry, we can cite: research and development of biocompatible surfactants and ionic liquids, the distribution and effect of surfactants and ionic liquids in the environment, development of non contaminant industrial processes, minimization, recycling and valorization of by-products and wastes of chemical industries. In the Nanotechnology area research is performed concerning adsorption and self-aggregation of surfactant as well as the physical chemistry and biophysics of natural lipids at interfaces and membranes (of natural origin or as physical chemistry models).

Research groups

- Minimization of Industrial Wastes: Isolation of High Added-Value Biopolymers
- Development of Non-contaminant industrial processes
- Statistical Modelling and Fibre Physics
- Biocompatible Surfactants
- Environmental Chemistry of Surfactants and Ionic Liquids
- Physical Chemistry of Surfactant Systems
- Biophysics of Lipids and Interphases

Minimization of Industrial Wastes: Isolation of High Added-Value Biopolymers

The main objective of our research main line is the design and development of medical devices for skin tissue regeneration and/or improving tissue function based on as bioactive materials of natural origin. Animal waste from food: meat, fish, poultry industries (slaughterhouse) and tanning industries will be used as raw material. Furthermore, the following additional waste should be included: fish waste, such as fish skins of hake, monkfish, sole and rock sole, and eggshell membrane. Of especial interest is the possibility of extracting other high-added value products closely related to collagen, glycosaminoglycans (GAGs) (dermatan sulfate, keratan sulfate, etc.) mainly from the meat and poultry industry (rooster combs, vitreous humour, synovial fluid) (5, 6) with hyaluronic acid as a maximum representative given its increasing use in medicine. It is expected to develop new medical devices for the rapid healing of the skin injuries (burns, ulcers, etc) that have not been resolved to date. Growing numbers of elderly people in Europe suffer from skin injuries such as bedsores and vascular ulcers and need effective medical devices that can be applied in hospitals and at home.

STAFF

JAUME COT COSP, GROUP LEADER

Publications (articles)

Magnetically separable nanocomposites with photocatalytic activity under visible light for the selective transformation of biomass-derived platform molecules

A.M. Balu, B. Baruwati, E. Serrano, J. Cot, J. Garcia-Martinez, R.S. Varma, R. Luque, Green Chem. 2012,13, 2750-2758.

.....

Tailor-made biopolymers from leather waste valorisation.

M. Catalina, J. Cot* A.M. Balu, J.C. Serrano-Ruiz, R. Luque, **Green Chem.**2012, 14, 308-312.

.....

Carbonaceous residues from biomass gasification as catalysts for biodiesel production

R. Luque*,A. Pineda, J.M. Campelo, J.C. Colmenares, A.A. Romero, J.C.Serrano-Ruiz, L.F. Cabeza, J. Cot, J. Natural Gas Chem., 2012, 21, 246-250.

.....

Microwave-assisted pyrolysis of biomass feedstocks: the way forward?

R. Luque* , J. A. Menendez, A. Arenillas, J. Cot, Energy Environ. Sci .

2012, 5, 5481-5488.

.....

From waste to healing biopolymers: biomedical applicatons of bio-collagen extracted from industrial residues in wound healing.

M. Catalina, J. Cot* M. Borras, J. De Lapuente, J. Gonzalez, A.M. Balu, R.Luque, Materials 2013, 6, 1599-1607.

.....

CO_2 sequestration properties of porous carbonaceous materials from leather residues.

J.M. Bermudez, P. Haro-Dominguez, A. Arenillas, J. Cot, J. Weber, R. Luque*, Materials 2013, 6, 4641-4653.

Research highlights

TAYLOR-MADE BIOMATERIALS FROM COLLAGENIC WASTES: FEASIBLE LINK BETWEEN TANNING INDUSTRY AND TISSUE ENGINEERING

The environment is one of the most relevant topics nowadays, the ecological conscience and the practice of an environmentally friendly and sustainable policy is increasing day by day all over the world. The concept of "Sustainable Development" transmits the idea of the rational use of the resources, the improvement of life quality and the maintenance of the ecosystems without jeopardising future generations. The improvement of the manufacturing processes, the finding of new types of renewable energies, the application of "clean" technologies in the processing, t the finding of new treatments for each type of waste; are essential steps to make compatible industrial development, environmental protection and social welfare. Waste treatments, in addition of reduce the volume of industrial waste could increase their value through the production of high added value products, entailing a great progress in both, environmental and economical terms.

In terms of waste generation, the production of leather gives rise to significant quantities of solid waste product for which tanneries are responsible for the cost of disposal and since most of this waste ends up in landfill it may be considered an environmental problem. However such waste is not without some potential value since it contains collagen which could be recycled and reused. Collagen is a very versatile and special high-added value protein and the most abundant and ubiquitous in vertebrates. This collagenic nature of the tannery solid waste permits us to think about treatments for obtaining biopolymers of reconstituted collagen, and their use in a wide range of potential applications.

Up to now, "low cost" biomaterials have been obtained. Their main applications have been: as filler, re-tanning agents and finishing agents in the tanning industry itself; and as a binder in the paper industry, partially substituting casein (much more expensive). The objective of the present work is the extraction, characterisation, optimisation and application of new "Taylor-made" smart biopolymers with high-added value, finding a new and feasible link between solid tannery waste and the rising market of tissue engineering.

Tissue engineering can be defined as an interdisciplinary field which applies, for one side, the principles of tissue engineering and, for another side, the sciences of life, with the aim of obtaining "Biological Structures" in order to regenerate and/or improve the tissue function. Although lots of synthetics biodegradable or bio-stable polymers have been employed on these "special structures", the affinity of the grafted cellules is quite low. Biologically derived materials are advantageous in that they contain information that facilitates cell attachment and function, whereas synthetics may not interact with cells in the desired manner[4]. The importance and special appeal of collagen as a biomaterial is based on the fact that collagen is a natural material and therefore it is assimilated by the human/animal body as a normal constituent and not as a foreign material, subjected to rejection, with a minimum of inmunogenicity. A great competitiveness of reconstituted collagen fibres in the field of regenerative medicine (tissues and/or organs) has been found in literature[4].

Biopolymers are polymers generated from renewable resources, often biodegradable and from non-toxic production. They can be produced from biological systems or chemically synthesised from biological raw materials. They are an alternative to the petrol-based polymers. The main problems of biopolymers are bio-compatibility, mechanical properties and adaptability. Collagenic biopolymers present huge possibilities due to the possibility of manufacture, and application, in different ways, forms and shapes, with well determined characteristics. We can talk about "Taylor-made" biopolymers: it is possible to produce easily said biopolymers as gel, film, fibres, tissue and/or sponges, using techniques such as freeze drying/lyophilisation, extrusion, or electro-spinning for nano-fibres formation.

In addition to the technical and scientific benefits obtained from the isolation of biopolymers from solid waste, this research could entail different economical benefits: In the first place, it presents a solution to a problem of dumping/storage of wastes, avoiding taxes for accumulating those wastes. Secondly, whole hides of low quality can be used as raw material, those hides, catalogued as a 4^{th}-5^{th} class, would be used to produce low quality articles of very low price on the market; however, the biopolymer extracted from this hide would have a high-added value. Thirdly, the treatment process is simple and cheap; environmentally and economically much more plausible than other treatments such as incineration, landfilling, etc. Finally, a wide range of potential applications for the produced bioproducts could be taken into consideration; with specific applications on medicine, veterinary and/or cosmetics, expanding field nowadays.

The technology to be used on the development of this research is focused on the production of macro-fibres (extrusion) and nano-fibres (electro-spinning), films, sponges (lyophilisation) and different types of scaffold material for tissue engineering.

The use of mathematical experimental designs permits to study the degree of significance of the different variables and the corresponding interaction between them in the different processes for obtaining collagenic biopolymers. This ensures that the experimentation can be rationalised and the optimum determined, being able to achieve a controlled production of "Taylor-made" biopolymers for each specific application.

The versatile properties of collagen have made collagenic biomaterials one of the most useful materials for tissue engineering. Those biomaterials can be in the form of and shape of natural tissue, porous scaffolds/sponges, fibres and gels. Reconstituted collagen fibres, and fibre networs have been shown to be a competitive biomaterial for soft and hard tissue replacement due to their advantageous properties. Those fibres have been used as well as a suture material. It has been postulated that such fibres could be knitted or woven into fabrics, although the production is difficult due to the large amount of material required. The traditional process for formation of collagen fibres involved the extrusion of collagen dispersions into a fibre formation buffer and subsequent solvent dehydration, air-drying and crosslinking.

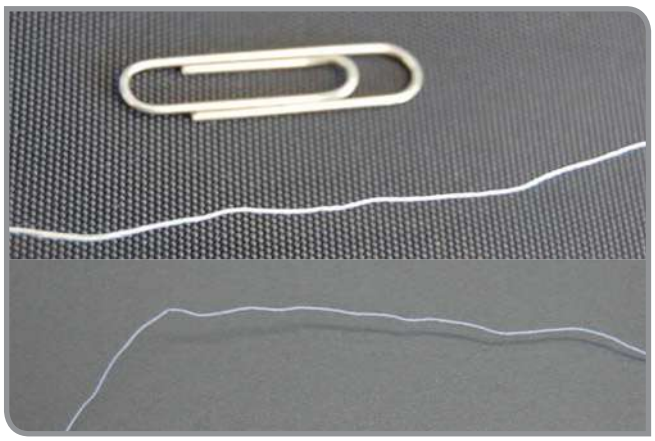


Fig. 1 and 2 Collagenic biopolymer extruded fibre.

Collagen sponges are generally formed by freeze-drying an aqueous collagen solution. The freeze-drying process includes freezing a collagen gel solution at a low temperature and subsequent sublimation of the ice crystals by vacuum at low temperature. The freezing temperature and freezing rate will have some effect on the porous structure of the resulting sponge.

Fig. 3 Collagenic biopolymer gel.

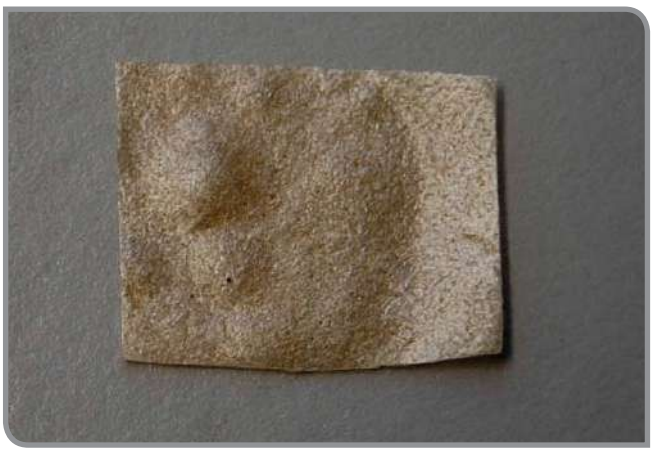


Fig. 4 Collagenic biopolymer film.

Fig. 5 Collagenic biopolymer sponge.

Industry implementation:

Figure represents the diagram of the industrial plant for the extraction and purification of collagenic biopolymers of different molecular weight fractions from tannery solid wastes. The basic steps of the process are as follows:

1st Step _ Grinding up Bovine Hides: Dried pickle bovine hides are ground up (grinder: J-110) into defibered small size (0.25 mm) and therefore giving a more homogeneous collagenic material with a greater surface, and consequently saving chemicals and shorten down the reaction time. Final product is impulsed through a pneumatic conveyor to the reactor.

2nd Step _ Production of collagenic biopolymers: The biopolymer extraction, the most important part of the whole process, is carried out in a stainless steel jacketed stirred reactor (R-120). The grounded hide is submitted to a mild controlled hydrolysis reaction; then, by means of a pump (P-121) is driven to filter unit (S-125), where the suspension particles are separated from the viscous collagenic solution.

3rd Step _ Ultrafiltration: The ultrafiltration is carried out by a combined sequentially connected set of three membrane-based tangential flow filtration spiral-wound modules of different cut-off ranges: 1kDa (U-141); 50kDa (U-142) and 100kDa (U-143). In each one of these subunits, the retentate fraction feeds the next subunit and the correspondent permeate fraction is kept apart. At the end of this 3rd step, four molecular weight collagenic biopolymer fractions were isolated: 1kDa; 1–50 kDa; 50–100kDa and over 100kDa.

4th Step _ Freeze-Drying: Each one of the four ultrafiltration fractions must be freeze-dried (lyophilisation) in order to keep their original structural and chemical properties. As shown on Figure 7, each unit of lyophilisation equipment was composed by the following parts: freezer (D-); condenser (E-); vacuum pump (V-) and storage tanks (T-).

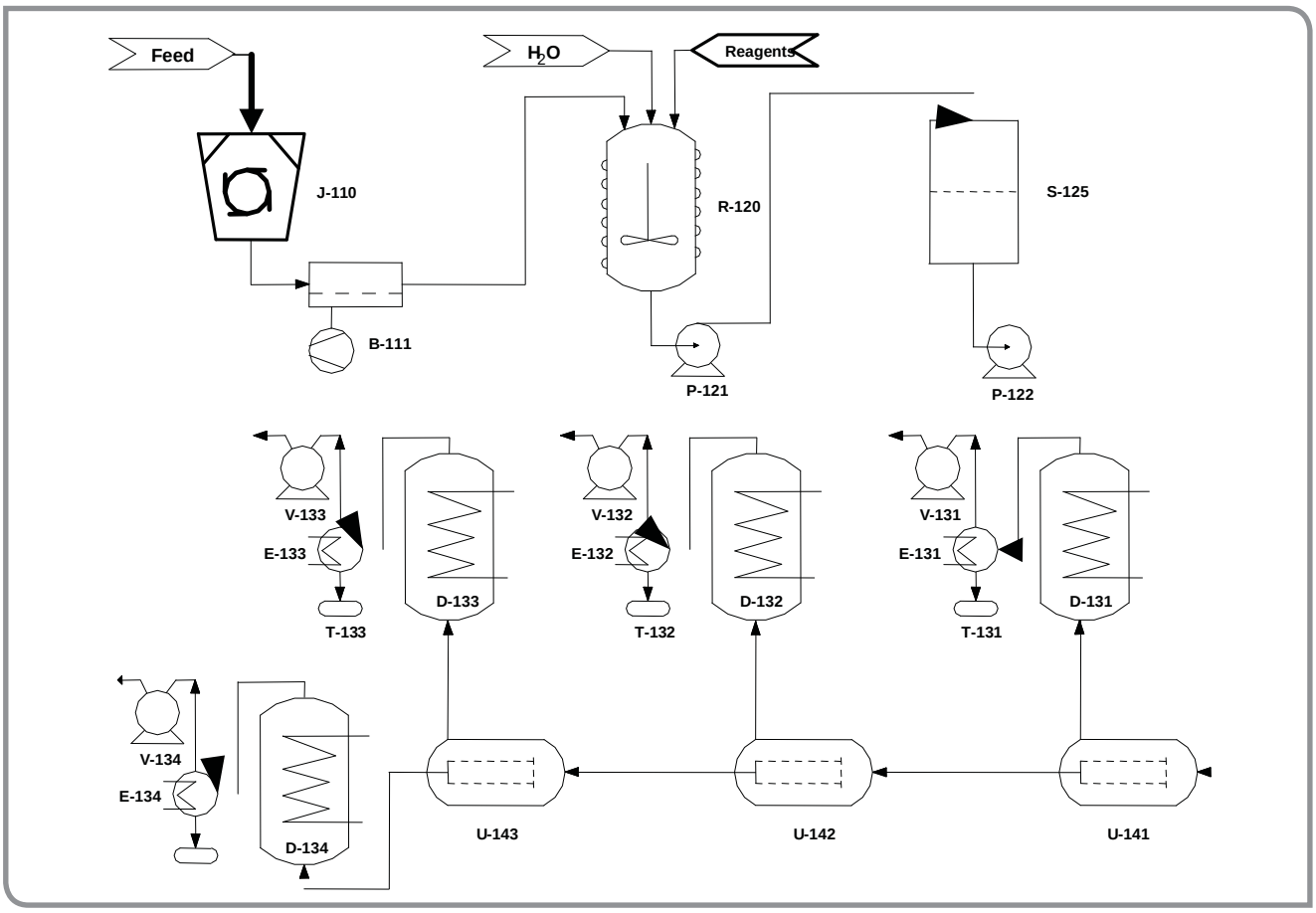


Fig.7 Scheme of the industrial plant for the processing of biopolymer extraction and purification.

Development of Non-Contaminant Industrial Processes

The research activities of the group are focused to develop and implement cleaner technologies to attain a more environmentally friendly leather industry and to study and develop end-of-pipe approaches to eliminate the main pollutants present in tannery waste waters in an attempt to reduce the contamination produced. The development and implementation of instrumental techniques for the analysis of the main chemicals involved in the leather manufacturing process is another research activity of the group

STAFF

AGUSTÍ MARSAL MONGE, GROUP LEADER
FERNANDO MALDONADO MILLÁN (hasta 30-04-2012)

Ph. D. STUDENTS

MARÍA ELENA BAUTISTA PÉREZ (hasta 31-12-2012)
SARA CUADROS DOMÉNECH (hasta 31-12-2012)

Publications (articles)

Alternative fungicides for the leather industry: Application in various processes.

Cuadros S, Manresa M, Font J, Bautista ME, Puig R, Marsal A.

J Soc. Leath Tech. Ch, 96, (6), 225-233, 2012

.....

Adsorption isotherm, thermodynamic and kinetics studies of polyphenols onto tannery shavings.

Marsal A, Maldonado F, Cuadros S, Bautista ME, Manich AM.

Chem Eng J 183, 21– 29, 2012

.....

Characterization of the volatile organic compounds by HS-SPME-CG-MS in the leather sector.

Cuadros RM, Marsal A, Ollé L, Bacardit A, Font J.

J Am Leath Ch Assoc., 108(11), 420-427, 2013

.....

Novel approach or the removal of organic contaminants inwastewaters: Adsolubilization of 2-naphthol onto collagen fibres.

Maldonado F, Manich AM, Marsal A.

J Soc Leath Tech Ch, 97, 105-110, 2013

.....

Use of modified leather shavings in the adsolubilization of 2-naphthol: Thermodynamic and kinetics studies.

Marsal A, Bautista ME, Manich AM, Cuadros S, Maldonado F.

Chem Eng J, 222, 77-84, 2013

.....

Determination of fungicides in residual tanning floats using solid phase micro extraction.

Font J, Reyes M, Cuadros S, Bacardit A, Ollé LL, Marsal A.

J Am Leath Ch Assoc., 108(2), 41-47, 2013

Research Projects

Tecnologías limpias en tenería: aplicación de nuevos compuestos fungicidas medioambientalmente sostenibles

Nacional, CTQ2009-08347

160.930 euros

2010-2012

Research highlights

Strict environmental legislation obliges tanners to adapt their processes to alternative technologies in order to minimize the environmental impact. This includes the search for new fungicide compounds that are less toxic, more environmentally friendly and cost effective. In a previous work, the fungicidal capacity of alternative fungicides (diiodomethyl-p-tolylsulfone (DIMPTS), 3-iodo-2-propynyl-N-butylcarbamate (IPBC) and 2-thiazol-4-yl-1H-benzo imidazole, thiobendazole (TBZ)) against different strains of fungi was compared to that of conventional compounds used in tannery (TCMTB and a mixture of phenolic compounds). It was found that two of them (DIMPTS and IPBC) could be satisfactorily used in tannery since their protection capacity for chrome leather was higher than that provided by the conventional compounds. In a more recent work, the use of these compounds was extended to other operations (fatliquoring process of vegetable tanned hides and preservative pickling process) of the transformation process of hides into leather. The results confirmed that these two compounds could be satisfactorily used not only in the chrome tanning process but also in the fatliquoring process of vegetable leather and in the preservative pickling process. The alternative fungicide compounds (DIMPTS and IPBC) showed a greater antifungal capacity and a lower toxicity than that of the conventional compounds.

In the application of any chemical in the different operations of leather manufacture, the quantification of the amount of the chemical that ends up in the wastewater is of paramount importance to assess its environmental impact. We have developed a method that enables us to determine quantitatively and simultaneously six fungicides contained in the residual floats. This method is based on solid-phase micro-extraction and liquid chromatography-photo diodes array detection. This very sensitive and highly specific method avoids the use of hazardous materials like solvents and does not generate significant laboratory wastes.

With the aim of developing innovative instrumental techniques, a very rapid and sensitive method has been developed for the characterization of the volatile organic compounds in the leather industry. The method consists of two steps. In the first one, headspace-solid phase micro extraction (HS-SPME) is used for the extraction of volatile and semi-volatile organic compounds, which are present in leather samples. The extracted compounds are determined by gas chromatography and its coupling with mass spectrometry (GC-MS) in the second step.

Surfactants are adsorbed in the solid/liquid interface in the form of aggregates known as admicelles by a process of self-assembly. In turn, admicelles can incorporate, also by a process of self-assembly, other molecules, neutral or ionized, that do not adsorb spontaneously to solid-water interfaces. This important solubilization phenomenon has been termed adsolubilization. Adsolubilization has been confirmed as a suitable tool to remove organic contaminants from waste waters. This important solubilization phenomenon may take place on fibrous collagen. The adsorption of the anionic surfactants sodium dodecyl sulphate and sodium dodecylbenzene sulphonate, respectively, onto hide powder collagen in an aqueous acidic medium allowed the adsolubilization of 2 naphthol, which in the absence of the surfactant is barely adsorbed to the protein. The maximum 2-naphthol adsolubilization took place at a pH value of 2-3. The thermodynamic study of the process, which obeyed a pseudo-second order model, revealed that this was exothermic, spontaneous and with decreased degree of freedom of the system.

Instead of using hide powder collagen, it has been proved that a waste of the leather industry, leather shavings (chrome and wet-white shavings) are also suitable as substrates in the removal of organic pollutants from waste waters through the adsolubilization process. The knowledge acquired on the adsolubilization phenomenon opens the door to a better understanding of some technological processes of leather manufacturing.

Statistical Modelling and Fibre Physics

Research work is focussed on the study of structure-property relationships of natural, synthetic and sustainable fibrous materials, particularly with regard to thermal, mechanical, viscoelastic and relaxation behaviour. The influence of novel more sustainable industrial processing on the structure and properties of fibrous materials are also taken into account.

STAFF

ALBERT M MANICH BOU, GROUP LEADER

TECHNICIANS

CARMEN FERRERO VIRGOS
BÁRBARA BAENA PÉREZ
DANIEL LÓPEZ SANTANA
JOAN LLORIA TOLRÀ

Publications (articles)

Microstructure variations of polylactide fibres with texturing conditions.

Cayuela D, Montero L, Díaz J, Algaba I, Manich AM.
Textile Res J, 82, 1996-2005, 2012

.....

Adsorption isotherm, thermodynamic and kinetics studies of polyphenols onto tannery shavings.

Marsal A, Maldonado F, Cuadros S, Bautista ME, Manich AM.
Chem Eng J 183, 21– 29, 2012

.....

Novel approach or the removal of organic contaminants inwastewaters: Adsolubilization of 2-naphthol onto collagen fibres.

Maldonado F, Manich AM, Marsal A.
J Soc Leath Tech Ch, 97, 105-110, 2013

Relationship between microstructure and properties of false-twist textured and stabilized polylactide. Part 2. physicochemical characterization, accessibility of the amorphous phase and dyeing behavior.

Cayuela D, Montero L, Riva A, Prieto R, Marti M, Manich AM.
Textile Res J, 83(10), 1065-1074, 2013

.....

Relationship between microstructure and properties of false-twist textured and stabilized polylactide. Part 1: Dimensional stability, mechanical properties and thermomechanical behavior.

Cayuela D, Montero L, Riva A, Prieto R, Cano F, Manich AM.
Textile Res J, 83(10), 1055-1064, 2013

.....

Use of modified leather shavings in the adsolubilization of 2-naphthol: Thermodynamic and kinetics studies.

Marsal A, Bautista ME, Manich AM, Cuadros S, Maldonado F.
Chem Eng J, 222, 77-84, 2013

.....

Determination of fungicides in residual tanning floats using solid phase micro extraction.

Font J, Reyes M, Cuadros S, Bacardit A, Ollé LL, Marsal A.
J Am Leath Ch Assoc., 108(2), 41-47, 2013

Moisture sorption/desorption of protein fibres.

Barba C, Martí M, Carilla J, Manich AM, Coderch L.
Thermochimica Acta, 552, 70– 76, 2013

Research Projects

Cinéticas de sorción/desorción de humedad y distribución de tamaño de poro en fibras vegetales

201280E035
2011-2014

.....

Composites de altas prestaciones de nanoparticulas ceramicas en fibras de poliester: propiedades y aplicaciones

MAT2010-20324-C02-02
2011-2014

.....

Valoración objetiva de propiedades, condiciones de mantenimiento y reciclado de diversos tipos de cesped artificial para optimizar sus prestaciones.
2010-2012

Research highlights

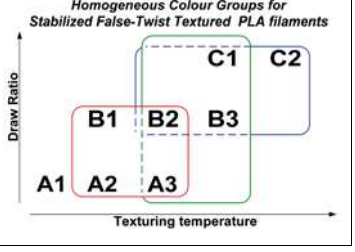
Fine structure of polylactide multifilaments after stabilisation and dyeing

Polylactides (PLA) are biodegradable, biocompatible and hydrolysable aliphatic polyesters that can be wholly obtained from renewable resources. Nature derived lactides are mostly in L-lactide form and exhibit crystalline behaviour. The microstructure of the multi-filaments is not easy to be controlled. As regards the industrial application of polylactide filaments the most important objective has been focused on the stabilisation of filaments considering the dimensional stability and the evolution of mechanical properties and dyeing behaviour.

It has been observed that stabilization increases crystallinity and orientation of the textured filaments with the result that the samples are more uniform for both parameters. The differences in the accessibility of the amorphous phase measured by the maximum phase lag temperature determined by TMA remain.

After stabilization the effect of the texturing draw ratio and that of the texturing temperature in dye absorption remain. The higher the texturing intensity, the lower the dye absorption. Differences in dye absorption can result in unacceptable colour value differences ΔE>1. Despite stabilization, PLA filaments false-twist textured under different conditions can cause dyeing irregularities when mixed in a fabric.

Sample	E	Homogeneous Colour Groups ΔE<1				
A1	53.37	X				
A2	54.41		X			
B1	54.66		X			
A3	54.95		X	X		
B2	55.17		X	X	X	
B3	55.67			X	X	
C1	55.84			X	X	
C2	56.00				X	

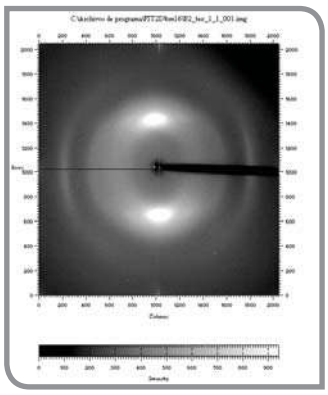


Iodine sorption and differential solubility show a good linear relationship with crystallinity: The higher the crystallinity, the lower the iodine sorption and the differential solubility.

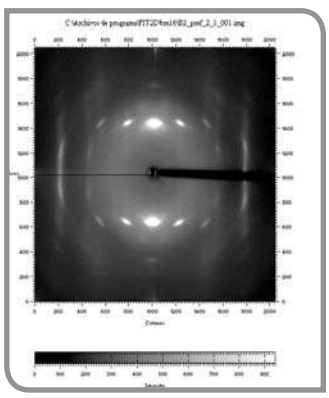
Although iodine sorption and differential solubility show higher sensitivity than crystallinity and/or orientation in differentiating between substrates, the maximum phase lag temperature and the sonic velocity enabled us to predict the colour value E of the stabilized false-twist textured filaments, allowing us to discriminate between acceptable and non acceptable colour differences. The higher the orientation and the lower the accessibility of the amorphous phase, the lower the dye absorption.

The strong relationship between differential solubility and iodine sorption with the maximum phase lag temperature highlights the influence of texturing temperature on filaments textured at the highest draw ratio when compared with other filaments textured under smoother conditions.

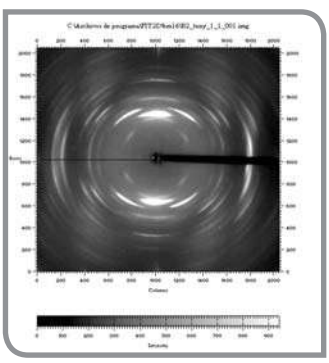
The increase in crystallinity after stabilization and dyeing can be clearly observed in the following XRD diagrams:



Textured substrate



Stabilized substrate



Dyed substrate

Biocompatible Surfactants

The activity of this research group deals with the fundamental and applied chemical investigation of novel environmentally friendly surfactants (products and processes) from natural renewable sources (proteins, polysaccharides, amino acids and natural oil derivatives), as alternatives to conventional surfactants to be applied in cosmetic, textile, dermopharmaceutical medical and food industrial preparations. These compounds can be classified as specialty surfactants with biodegradable, antimicrobial and low toxicity profiles, and characteristic self-aggregation properties. The objectives are focused on the preparation of safer and healthier surfactants using molecular design and the principles of toxicity and environmental mechanism of action to minimise the intrinsic toxicity/ecotoxicity of the product while maintaining its efficacy and function. This line is loosely-bound with applied surface chemistry and biological area. It is active in the following tasks: the use of renewable raw materials for the synthesis of surfactants: proteins, polysaccharides, triglycerides; Employing natural processes using biocatalyst based chemical transformations (enzymes) for efficiency and selectivity; the use of safer solvents (water systems, solvent-free processes, Ionic liquids, etc.); study of mechanism of cellular action; novel functionality: bio/nano materials; self-assembling and ecotoxicity characterization.

STAFF

Mª ROSA INFANTE MARTÍNEZ-PARDO, GROUP LEADER
LOURDES PÉREZ MUÑOZ
AURORA PINAZO GASSOL

Ph. D.

LORENA TAVANO

Ph. D. STUDENTS

MARTA BUSTELO

VISITING PROFESSOR

MARIA DEL CARMEN FLORIDO

LEONARDO DA VINCI STUDENTS

VALERIA PETTRIZELLI

TRAINING STUDENTS

CAMILLE BIRENBAUM
CLAIRE BOURGAREL
CHARLENE LOUIS
JANA ALBOQUERS
ESTAFANIA CARRASCO

Publications (articles)

Bio-based Surfactants from Renewable Resources

Soft-Journal, 138, 37-44, 2012

M.R. Infante, L. Pérez, A. Colomer, M.C. Morán, R. Pons, M.T. García A. Pinazo

.....

Membrane-destabilizing activity of pH-responsive cationic lysine-based surfactants: role of charge position and alkyl chain length.

Nogueira DR, Mitjans M, Moran MC, Pérez L, Vinardell MP.

Amino Acids, 43, 1203–1215, 2012

.....

Self assembly of pH-sensitive cationic lysine based surfactants.

Mezei A, Pérez L, Pinazo A, Comelles F, Infante MR, Pons R.

Langmuir, 28, 16761–16771, 2012

.....

Surface activity and aggregation of pristine and hydrophobically modified inulin.

Morros J, Infante MR, Pons R.

Soft Matter, 8, 11353-11362, 2012

.....

Thermoresponsive hydrogels with low toxicity from mixtures of ethyl(hydroxyethyl) cellulose and arginine-based surfactants.

Calejo MT, Kjoniksen A-L, Pinazo A, Pérez L, Cardoso AMS, Pedroso De Lima MC, Jurado AS, Sande SA, Nyström B.
Int. J. Pharm, 436, 454– 462, 2012

Phospholipid bilayer-perturbing properties underlying lysis induced by pH-sensitive cationic lysine-based surfactants in biomembranes.

Nogueira DR, Mitjans M, Busquets MA, Pérez L, Vinardell MP.

Langmuir, 28, 11687–11698, 2012

Ribbon-type and cluster-type lipoplexes constituted by a chiral lysine based cationic gemini lipid and plasmid DNA.

Barrán-Berdón AL, Muñoz-Úbeda M, Aicart-Ramos C, Pérez L, Infante MR, Castro-Hartmann P, Martín-Molina A, Aicart E, Junquera E.

Soft Matter, 8, 7368-7380, 2012

pH-sensitive surfactants from lysine: assessment of their cytotoxicity and environmental behavior .

Colomer A, Pinazo A, García MT, Mitjans M, Vinardell MP, Infante MR, Martínez V, Pérez L.

Langmuir, 28, 5900–5912, 2012

Mixed monolayer of DPPC and lysine-based cationic surfactants: An investigation into the antimicrobial activity.

Colomer A, Perez L, Pons R, Infante MR, Perez-Clos D, Manresa A, Espuny MJ, Pinazo A.

Langmuir, 29(25), 7912–7921, 2013

Synthesis and physico-chemical studies of ester-quat surfactants in the series of (dodecanoyloxy)propyl n-alkyl dimethyl ammonium bromide.

Achouri ME, Alehyen S, Assioui A, Chami R, Bensajjay F, Pérez L, Infante MR.

J. Surfact. Deterg., 16, 473–485, 2013

Aggregation behavior and antimicrobial activity of ester-functionalized imidazolium- and pyridinium-based ionic liquids in aqueous solution.

Garcia MT, Ribosa I, Perez L, Manresa A, Comelles F.

Langmuir, 29, 2536-2545, 2013.

In vitro antitumor activity of methotrexate via pH-sensitive chitosan nanoparticles.

Nogueira DR, Tavano L, Mitjans M, Pérez L, Infante MR, Vinardell MP.
Biomaterials, 34, 2758-2772, 2013

New cationic nanovesicular systems containing lysine-based surfactants for topical administration: Toxicity assessment using representative skin cell lines.

Nogueira DR, Morán MC, Mitjans M, Martínez V, Pérez L, Vinardell MP.
Eur J Pharm Biopharm, 83, 33–43, 2013

Role of aggregate size in the hemolytic and antimicrobial activity of colloidal solutions based on single and gemini surfactants from arginine.

Tavano L, Infante MR, Riya MA, Pinazo A, Vinardell MP, Mitjans M, Manresa MA, Perez L.
Soft Matter, 9, 306-319, 2013

Research Projects

Tensioactivos poliméricos antimicrobianos preparados a partir de biopolímeros y tensioactivos catiónicos derivados de aminoácidos

Nacional, MAT2012-38047-C02-02
2013-2015

Estudios orientados a mejorar la seguridad de sistemas tensioactivos catiónicos de lisina

Nacional, CTQ2009-14151-C02-01
2010-2012

Ayudas para apoyar las actividades de los grupos de investigación para el año 2009. Nombre del grupo: Tensioactius i química sostenible

Generalitat, 2009SGR1331
2009-2014

Food Waste Valorisation (EUBis Action), COST ACTION TD1203

EUBis COST Action. Enero 2013-Diciembre 2016

Control y aplicación de nanoestructuras formadas por sistemas tensioactivos catiónicos biocompatibles derivados de lisina

CTQ2010-2013-14897

Research highlights

Novel high-quality components of consumer friendly market products require sustainable surfactants with multifunctional characteristics such as: biodegradability, mildness, low potential toxicity, water solubility, and wide range of hydrophilic-lipophilic balance. In this context the research of biocompatible surfactant group is related with the search of new biocompatible surfactants derived from amino acids.

It has been shown that cationic amphiphiles have great potential in biomedical applications as antimicrobial and antifungal agents in human infections. They can also be used in gene therapy, as vehicles for certain drugs, and as modifiers of the physicochemical and biological properties of biomaterials.

In the last two years, our efforts have been directed towards the exploration of possible applications of cationic surfactants derived from amino acids. Two types of surfactants have been studied, cationic surfactants with one fatty chain and gemini surfactants. The results achieved are highlighted below.

Lysine based surfactants with one fatty chain

Our group has recently synthesized cationic surfactants of the type Nε -acyl lysine methyl ester hydrochloride salts for which the alkyl chain length has been varied from 12 to 16 carbon atoms. These surfactants have the cationic charge on amine protonated groups, consequently depending on the pH value, these surfactants can dissociate in aqueous solutions, losing the cationic charge. Their protonation constant were determined by potentiometric titration. The obtained pKa values indicate that these surfactants have weak acidic properties; consequently, the cationic character will depend on the pH of the medium. This behavior could be interesting in medicinal chemistry, because changes in the protonation state of pH-tritable headgroups would lead to changes in the headgroup area and, as a result, in their aggregation state. Surfactants with this type of behavior have been shown to be efficient vectors for gene therapy because the release of DNA into the cells is improved and, consequently, the level of gene transfection may be increased.

The ability to disrupt the cell membrane in a range of pH values, surfactant concentration and incubation time was also studied. For these studies standard hemolysis assay as a model of endosomal membranes has been used. Although all surfactants enhanced hemolysis with increasing concentration, only the compound with the positive charge on α-amino group of lysine showed pH-responsive hemolityc activity. An increase in the alkyl chain length carbon atoms lowered the ability to disrupt cell membranes. The mechanism of biomembrane lysis was shown to be associated with lipid bilayer disorganization, through interaction with lipids and proteins of the membrane. It was also shown that the phospholipid bilayer-perturbing properties of these surfactants depend on their structural features. Hence, the pH-dependent membrane-disruptive activity can be fine-tuned mainly by varying the position of the cationic charge and and by changing the length of the alkyl chain.

Cationic nanovesicles have attracted considerable interest as effective carriers to improve the delivery active molecules into and through the skin. Lipid-based nanovesicles containing lysine based surfactants were designed for topical administration. A representative skin cell lines and in vitro assays was used to assess whether the cationic compounds modulate the toxic responses of these nanocarriers. No potential phototoxicity was detected in fibroblast or keratinocyte cells, whereas only sligth inflammatory response was detected.

Gemini arginine based surfactants

Ethyl(hydroxyethyl)cellulose (EHEC) is known to form hydrogels in water at elevated temperatures in the presence of an ionic surfactant. The potential use of arginine based surfactant was explored considering the production of a low toxicity thermoresponsive hydrogel for pharmaceutical and biomedical applications. Both the monocatenary and two gemini surfactants were found to induce gelation of semidilute EHEC solutions as the temperature is increased. Considering a pharmaceutical or medical applications, these systems are suitable candidates for the administration as a liquid solution (at low temperatures), undergoing in situ gelation at body temperature.

Gemini lysine based surfactants

The toxicity and environmental behavior of new pH-sensitive surfactants from lysine has been studied. Three different chemical structures were studied: surfactants with one amino acid and one alkyl chain, surfactants with two amino acids on the polar head and one alkyl chain, and gemini surfactants. The pH sensitivity of these compounds can be tuned by modifying their chemical structures. Cytotoxicity has been evaluated using erythrocytes and fibroblast cells. The toxic effects against these cells depend on the hydrophobicity of the molecules as wells as their cationic charge density. The effect of hydrophobicity and cationic charge density on toxicity is different for each

type of cells. For erythrocytes, the toxicity increases as hydrophobicity and charge density increases. For fibroblast cationic charge density affects cytotoxicity in the opposite way: the higher charge density, the lower the toxicity. The aquatic toxicity was established using Daphnia magna. All surfactants tested are considerably more biodegradable than that reported for cationic surfactants based on quaternary ammonium groups.

Also antimicrobial activity vas evaluated. With the aim to elucidate the mechanisms involved in the antimicrobial activity a simple membrane model (DPPC monolayer) was used. Compression isotherms of mixtures of DPPC/lysine surfactants at different pH showed an expansion of the DPPC monolayer, suggesting cationic lysine surfactant/DPPC interactions, which strongly depend on surfactant structure and hydrophobic interactions. Antimicrobial activity of the three surfactants has also been assessed with transmission electron microscopy, observing the effects on the microorganisms. The three surfactants caused various kinds of damage to the bacteria tested, such as structural alterations, leakage of internal material, and cell destruction.

Environmental Chemistry of Surfactants and Ionic Liquids

The main objective is the study of the physicochemical and biological properties related to the behaviour, fate and effects of surfactants and ionic liquids in the environment for the design and selection of efficient and environmentally friendly compounds. Our research activities are mainly focused on the bioavailability, biodegradability and toxicity of surfactants and ionic liquids in the aquatic environment.

STAFF

MARÍA TERESA GARCÍA RAMÓN, GROUP LEADER
FRANCESC COMELLES FOLCH

TECHNICIANS

ISABEL RIBOSA FORNOVI
JUAN JOSÉ GONZÁLEZ CHAPARRO
ISABEL MUÑOZ LIRÓN
ROSA MARÍA SALVIA PEIRÓ

STUDENTS

ALICIA SEDOUI
MAGALIE CARCILLO
FIORA BOURGES
EMELINE CALAFELL

Publications (articles)

Self assembly of pH-sensitive cationic lysine based surfactants.

Mezei A, Pérez L, Pinazo A, Comelles F, Infante MR, Pons R.

Langmuir, 28, 16761−16771, 2012

.....

Interaction of nonionic surfactants and hydrophilic ionic liquids in aqueous solutions: Can short ionic liquids be more than a solvent?.

Comelles F, Ribosa I, González JJ, Garcia MT.

Langmuir, 28, 14522-14530, 2012

.....

Antimicrobial toxicity studies of ionic liquids leading to a 'hit' MRSA selective antibacterial imidazolium salt.

Coleman D, Spulák M, Garcia MT, Gathergood N.

Green Chem., 14, 1350-1356, 2012

.....

pH-sensitive surfactants from lysine: assessment of their cytotoxicity and environmental behavior .

Colomer A, Pinazo A, García MT, Mitjans M, Vinardell MP, Infante MR, Martínez V, Pérez L.

Langmuir, 28, 5900−5912, 2012

.....

Interfacial behavior of chroman-6 and chroman-6 palmitoyl ester and their interaction with phospholipids.

García-Antón JM, Reig F, Messeguer A, Comelles F, Espina M, Alsina MA,

Colloid Polym Sci, 291, 1065–1075, 2013

.....

A new generation of aprotic yet Brønsted acidic imidazolium salts: effect of ester/amide groups in the C-2, C-4 and C-5 on antimicrobial toxicity and biodegradation.

Gore RG, Myles L, Spulak M, Beadham I, Garcia TM, Connon SJ, Gathergood N.

Green Chem.,15, 2747-2760, 2013

Aggregation behavior and antimicrobial activity of ester-functionalized imidazolium- and pyridinium-based ionic liquids in aqueous solution.

Garcia MT, Ribosa I, Perez L, Manresa A, Comelles F.

Langmuir, 29, 2536-2545, 2013

Research Projects

Tensioactius i Química Sostenible

AGAUR SGR-1331

2009-2013

Ayudas para la contratación de personal Técnico de Apoyo

MICINN, PTA2010-3813-I

2011-2013

Food Waste Valorisation

EUBis COST Action TD 1203

2013-2016

Estudios orientados a mejorar la seguridad de sistemas tensioactivos catiónicos de lisina

Nacional, CTQ2009-14151-C02-01

2010-2012.

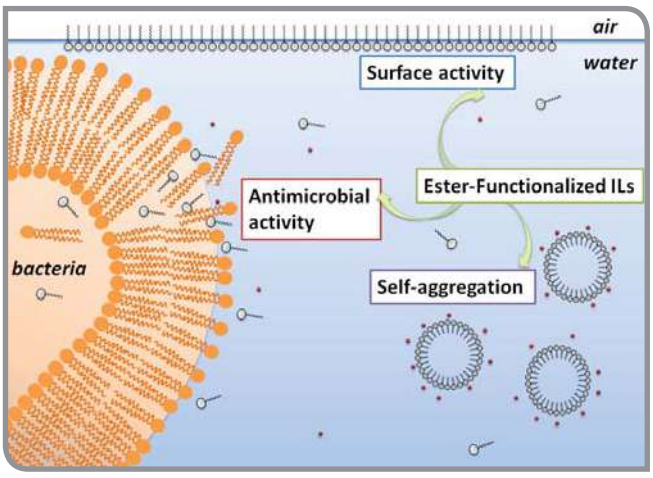
Research highlights

Self-aggregation and antimicrobial activity of functionalized ionic-liquids

The study of ionic liquids (ILs) as a new class of non-molecular, ionic solvents for use in sustainable processes as solvents, catalysts and electrolytes has increased exponentially during the last years. Most widely studied ILs are comprised of bulky, asymmetric N-containing organic cations in combination with any wide variety of anions, ranging from simple inorganic anions to more complex organic species. One of the main aspects gaining attention in ILs research is the enormous range of cation-anion combinations, which results in a large potential for adjustability of structure-properties. ILs are often called "designer solvents" or considered "task-specific" because of their possibility to be tailored to fulfill the technological demands of a variety of applications.

ILs emerged as a possible "green" alternative to common organic solvent due to extremely low vapor pressures. However, other release routes aside evaporation to the environment must be addressed before ILs can be considered as environmental acceptable compounds. Most of the commonly used ILs are not readily biodegradable compounds. Previous studies within our group have focused on synthesizing non-toxic ILs that undergo aerobic biodegradation as a pathway that represents a minimal environmental impact and a means of generating truly green compounds. Our studies on both imidazolium and pyridinium based ILs highlighted that the introduction of a cleavable ester functional group in the side chain leads to a significant increase of the biodegradability of the ionic liquid molecules in comparison to those ILs bearing simple alkyl chains. These encouraging data on the effect of the ester functionality on promoting IL biodegradability have led us to synthesize and investigate the self-aggregation and antimicrobial activity in aqueous solution of a series of long chain ILs containing a cleavable functional group.

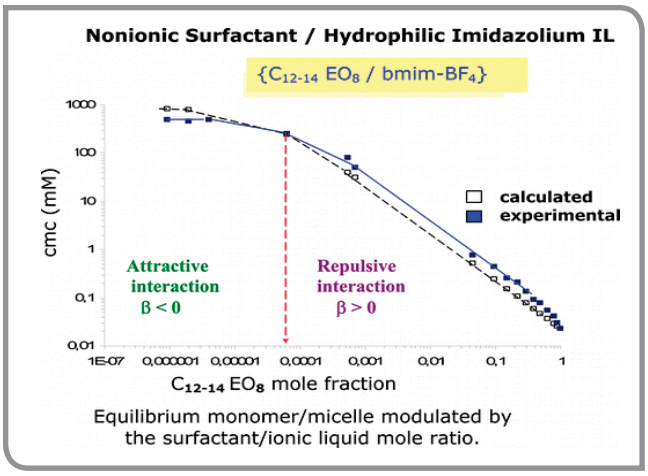
Our studies show that the introduction of a hydrolytically cleavable ester functionality not only improves IL biodegradation but also surface and biological activities of ILs. The better understanding of the structural parameters affecting self-aggregation and biological activity of the long chain ionic liquids is expected to aid in the design and selection of ionic liquids with improved physicochemical and biological properties for new pharmaceutical, engineering or nanotechnology applications.



Surfactant-like behavior and antimicrobial activity of long-chain ester-functionalized ionic liquids in water

Interactions between surfactants and ionic liquids

Accordingly with its claimed role as "green solvents", a wide series of studies where ILs are used as dilution media of conventional surfactants are reported in literature. Recently, we give evidence that even for short chain ILs, a process of aggregation in aqueous solution can take place. Consequently, when a surfactant is dissolved in an aqueous solution containing ionic liquid, the role of this compound as a secondary surfactant should also be considered. We claimed that these systems should be treated as typical binary surfactant systems in aqueous solution, in which case the phenomena of synergism frequently occur. The equations of the Regular Solution Theory can be applied to quantify the synergism by means of the interaction parameter β.



Equilibrium monomer/micelle modulated by the surfactant/ionic liquid mole ratio.

The surfactant parameters obtained are attributable not only to the surfactant but also to the mixed micelles formed between the surfactant and the ionic liquid. This approach can contribute to a better understanding of the experimental results reported where only the role of solvent is considered for ILs..

Physical Chemistry of Surfactant Systems

The general subject of research is the physical chemistry of surfactants and surfactant based systems. Particular focus is given to dynamic transformations (emulsification and solubilisation) and to new biocompatible surfactant behaviour. The main techniques are SAXS-WAXS, light scattering, tensiometry, conductivity and selective electrode.

STAFF

RAMON PONS PONS, GROUP LEADER

TECHNICIANS

JAUME CAELLES BALCELLS
IMMA CARRERA ALTARRIBA

Ph. D.

AMALIA MEZEI
JORDI MORROS CAMPS

Publications (articles)

Self assembly of pH-sensitive cationic lysine based surfactants.

Mezei A, Pérez L, Pinazo A, Comelles F, Infante MR, Pons R.

Langmuir, 28, 16761−16771, 2012

Surface activity and aggregation of pristine and hydrophobically modified inulin.

Morros J, Infante MR, Pons R.

Soft Matter, 8, 11353-11362, 2012

Bicellar systems to modify the phase behaviour of skin stratum corneum lipids.

Rodríguez G, Cócera M, Rubio L, Alonso C, Pons R, Sandt C, Dumas P, López-Iglesias C, de la Maza A, López O.

Phys. Chem. Chem. Phys., 14, 4523-14533, 2012

A unique bicellar nanosystem combining two effects on stratum corneum lipids

Rodríguez G, Cócera M, Rubio L, López-Iglesias C, Pons R, De La Maza A, López O.

Mol. Pharmaceutics, 9, 482−491, 2012

Protein-covered silica nano-particles adsorbing onto synthetic vesicles.

De Persiis F, La Mesa C, Pons R

Soft Matter, 8, 1361-1368, 2012

Structure and phase equilibria of the soybean lecithin/PEG 40 monostearate/water system.

Montalvo G, Pons R, Zhang G, Díaz M, Valiente M.

Langmuir, 29, 14369-14379, 2013

Extraction, purification and nanoformulation of natural phycocyanin (from Klamath algae) for dermal and deeper soft tissue delivery.

Caddeo C, Chessa M, Vassallo A, Pons R, Diez-Sales O, Fadda AM, Manconi M.

J. Biomed. Nanotech., 9(11), 1929-1938, 2013

Peptide nanofibres as molecular transporters: From self-assembly to in vivo degradation.

Mazza M, Patel A, Pons R, Bussy C, Kostarelos K.
Faraday Discuss., 166, 181-194, 2013

.....

The nanostructure of surfactant–DNA complexes with different arrangements.

Mezei A, Pons R, Morán MC.
Colloids Surfaces B: Biointerfaces, 111, 663– 671, 2013

.....

Mixed monolayer of DPPC and lysine-based cationic surfactants: An investigation into the antimicrobial activity.

Colomer A, Perez L, Pons R, Infante MR, Perez-Clos D, Manresa A, Espuny MJ, Pinazo A.
Langmuir, 29 (25), 7912–7921, 2013

.....

New chiral polyfunctional cyclobutane derivatives from (-)-verbenone: possible surfactant behaviour.

Ospina J, Sorrenti A, Illa O, Pons R, Ortuño RM.
Tetrahedron: Asymmetry 24, 713–718, 2013

.....

The production and physicochemical properties of a biosurfactant mixture obtained from Sphingobacterium detergens.

Burgos-Díaz C, Pons R, Teruel JA, Aranda FJ, Ortiz A, Manresa A, Marqués AM.
J Colloid Interface Sci, 394, 368–379, 2013

Research Projects

Control y aplicacion de nanoestructuras formadas por sistemas tensioactivos catanionicos biocompatibles

Nacional, CTQ2010-14897
2011-2013

.....

Evaluación de métodos físico-químicos para la reducción de la concentración de derivados sulfurados en hidrocarburos

Rofeica Energía, S.A.
2012-2014

Estudios de la reduccion de contaminante en un fuel recuperado
2012

Research highlights

The results during these two years can be divided into three main groups; those referring to phospholipid based vesicles, their characterization and use as drug delivery vehicles, those referring to other delivery systems and those referring to new surfactants and the characterization of the structures they form.

Several lipidic vesicles have been characterized, in particular looking for the effect of additives on the bilayer properties (thickness, polar-apolar distribution, lamellarity and elasticity).

Those other vehicles that have been the object of study and characterization include protein-inorganic nanoparticles and their interaction with vesicles, bicellar lipidic nanoparticles, peptide nanofibers and cationic surfactant-DNA complexes. In this last we have been able to measure the SAXS spectra of the complex while forming at the interface between DNA and cationic surfactant solutions and have compared this with the structure of the complex formed in gel particles at long times.Depending on the preparation procedure, the hexagonal packing of the structure is more or less evident (fig. 1)

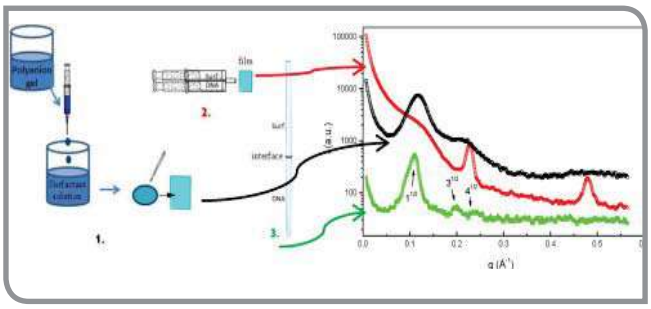


Figure 1. Three methods of DNA-Cationic surfactant complex formation and their respective SAXS spectra showing the diverse state of organization.

Concerning the study of new surfactants we have studied hydrophobically modified aminoacids and peptides (lipoaminoacids), hydrophobically modified polymeric sugars, hydrophobically modified non-natural aminoacids and also bio surfactants. All those chemical approaches have in common search for increased activity and biocompatibility with reduced environmental impact.

Special emphasis has been devoted to the study of the influence of pH on the aggregation and phase behavior. Because these surfactants have relatively complex polar heads with pH ionizable groups and multiple hydrogen bonding possibilities, the phase behavior is finely tuned by pH.

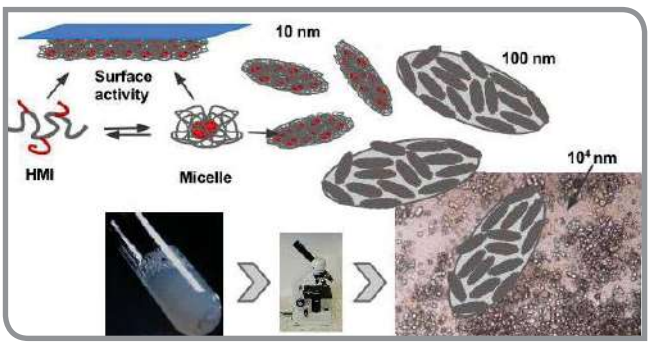


Figure 2. The several length scales at which the hydrophobically modified inulin surfactants self-assemble.

Polymeric based surfactants are attractive because they can be based on natural products adequately modified to provide them with distinct hydrophilic-hydrophobic moieties. Because of their origin, they do not show strong negative effect on the environment. In our research, we have determined several levels of self-aggregation of hydrophobically modified inulin oligomers (fig.2) that can be used as surfactants or as templates for the production of nanoparticles.

Finally, the research group actively seeks for the transfer of the basic knowledge generated to the productive sector. This interest is reflected in the presentation of two patents and research contracts with industry.

Biophysics of Lipids and Interphases

The main research lines of this group are: lipid assembling (liposomes, bicosomes, microspheres, micelles, bicelles and bilayers), lipokeratinic tissues (skin, wool and human hair), percutaneous absorption and physicochemical characterization of colloids with potential industrial applications.

STAFF

JOSÉ LUIS PARRA JUEZ, GROUP LEADER
Mª LUISA CODERCH NEGRA
ALFONS DE LA MAZA RIBERA
OLGA LÓPEZ SERRANO

TECHNICIANS

MERITXELL MARTÍ GELABERT
ISABEL YUSTE HERNÁNDEZ
VANESSA MARTÍNEZ RODRÍGUEZ

Ph. D.

CRISTINA ALONSO MERINO
CLARA BARBA ALBANELL
MERCEDES CÓCERA NÚÑEZ
LUCYANNA BARBOSA-BARROS
GELEN RODRÍGUEZ DELGADO
LAIA RUBIO TOLEDANO

Ph. D. STUDENTS

ESTIBALIZ FERNÁNDEZ PINTO

Publications (articles)

Efficacy of antioxidants in human hair.

Fernández E, Martínez-Teipel B, Armengol R, Barba C, Coderch L.

J. Photochem. Photobiol. B: Biology, 117, 146-156, 2012

.....

Bicellar systems to modify the phase behaviour of skin stratum corneum lipids.

Rodríguez G, Cócera M, Rubio L, Alonso C, Pons R, Sandt C, Dumas P, López-Iglesisa C, de la Maza A, López O.

Phys. Chem. Chem. Phys., 14, 4523-14533, 2012

.....

Development and characterization of a novel nystatin-loaded nanoemulsion for the buccal treatment of candidosis: ultrastructural effects and release studies.

Campos FF, Calpena Campmany AC, Delgado GR, Serrano OL, Naveros BC.

J Pharm. Sci., 101(10), 3739–3752, 2012

.....

A unique bicellar nanosystem combining two effects on stratum corneum lipids

Rodríguez G, Cócera M, Rubio L, López-Iglesias C, Pons R, De La Maza A, López O.

Mol. Pharmaceutics, 9, 482–491, 2012

.....

Monitoring of the microcapsule/liposome application on textile fabrics.

Martí M, Rodríguez R, Carreras N, Lis M, Valldeperas L, Coderch L, Parra JL.

J. Textile Inst., 103(1), 19-27, 2012

.....

Bicellar systems as a new colloidal delivery strategy for skin.

Rubio L, Rodríguez G, Barbosa-Barros L, Alonso C, Cócera M, de la Maza A Parra JL, López O.

Colloids and Surfaces B: Biointerfaces 92, 322– 326, 2012

Bicelles: Lipid Nanostructured Platforms with Potential Dermal Applications.

Barbosa-Barros L, Rodríguez G, Barba C, Cócera M, Rubio L, Estelrich J, López-Iglesias C, De La Maza A, López O.

Small, 8(6), 807–818, 2012

Laccases stabilization with phosphatidylcholine liposomes.

Martí M, Zille A, Cavaco-Paulo A, Parra JL, Coderch L.

J. Biophys. Chem. 3, 81-87, 2012

Photodamage determination of human hair.

Fernández E, Barba C, Alonso C, Martí M, Parra JL, Coderch L.

J. Photochem. Photobiol. B: Biology 106, 101–106, 2012

Cosmetotextiles with Gallic Acid: Skin Reservoir Effect.

Martí M, Alonso C, Martínez V, Lis M, de la Maza A, Parra, JL, Coderch L.

J Drug Delivery, 2013, Article ID 456248, 2013

Bicellar systems as new delivery strategy for topical application of flufenamic acid.

Rubio L, Alonso C, Rodríguez G, Cócera M, López-Iglesias C, Coderch L, De La Maza A, Parra JL, López O.

Int. J. Pharm., 444, 60–69, 2013

Keratins and lipids in ethnic hair.

Cruz CF, Fernandes MM, Gomes AC, Coderch L, Martí M, Méndez S, Gales L, Azoia NG, Shimanovich U, Cavaco-Paulo A

Int. J. Cosmetic Sci., 35, 244-249, 2013

Characterization of new DOPC/DHPC platform for dermal applications.

Rodríguez G, Rubio GL, Barba C, López-Iglesias C, de la Maza A, López O, Cócera M.

Eur. Biophys. J., 42, 333–345, 2013

Antioxidant cosmeto-textiles: Skin assessment.

Alonso C, Martí M, Martínez V, Rubio L, Parra JL, Coderch L.

Eur J Pharm Biopharm., 84, 192-199, 2013

Moisture sorption/desorption of protein fibres.

Barba C, Martí M, Carilla J, Manich AM, Coderch L.

Thermochimica Acta, 552, 70– 76, 2013

Drug release system of ibuprofen in PCL-microspheres.

Carreras N, Acuña V, Martí M, Lis M.

Colloid Polym. Sci., 291, 157-165, 2013

Hair Efficacy of Botanical Extracts.

Benaiges A, Fernández E, Martínez-Teipel B, Armengol R, Barba C, Coderch L.

J. Appl. Polym. Sci., 128, 861-868, 2013

Evaluation of novel nystatin nanoemulsion for skin candidosis infections.

Fernández-Campos F, Clares Naveros B, López Serrano O, Alonso Merino C, Calpena Campmany AC.

Mycoses, 56, 70-81, 2013

Relationship between microstructure and properties of false-twist textured and stabilized polylactide. Part 2. physicochemical characterization, accessibility of the amorphous phase and dyeing behavior.

Cayuela D, Montero L, Riva A, Prieto R, Marti M, Manich AM.

Textile Res J, 83(10), 1065-1074, 2013

Publications
(books and book chapters)

Water sorption of human keratinized fibers: effect of wool keratin proteins and peptides.

Barba C, Martí M, Roddick-Lanzilotta A, Manich AM, Carilla J, Parra JL, Coderch L. "Keratin Structure, Properties and Applications" (Ed. Renke Dullaart) 4, 89-111, 2012

.....

Bicelles: New nanosystems for skin applications

Barbosa-Barros L, Rodríguez G, Cócera C, Rubio L, Estelrich J, de la Maza A, López O.

Recent Advances in Pharmaceutical Sciences II (Transworld research Network) , chapter 8, 135-149, 2012

Research projects

Lavado en seco de lana eco-eficiente con recuperacion total de subproductos.

IPT-2012-0644-310000

2013-2015

.....

Eco-efficient wool dry scouring with total by products recovery

CCEE, LIFE11 ENV/ES/588

2012-2015

.....

Diseño, estabilizacion y optimizacion de nanoestructuras bicelares: aplicacion en entornos diluidos y efecto sobre las estructuras de la piel

Nacional, CTQ2010-16964

2011-2013

.....

Eficacia de antioxidantes en cabello humano

Nacional, TRA2009_02820

2010-2012

.....

Encapsulación lipídica/polimérica en la producción de tejidos biofuncionales.

Nacional, CTQ2009-13967-C03-01

1/1/2010-31/12/2012

Ayudas para apoyar las actividades de los grupos de investigación para el año 2009. Nombre del grupo: Físicoquímica i estructuració vesicular de lipids i biopolimers bacterians

Generalitat de catalunya, 2009SGR1212

2009-2014

.....

Desarrollo de una formulación que estabilice la fosfomicina y aumente la biodisponibilidad del antibiótico

CDTI- LABIANA SA

2013-2015

.....

Preparación y caracterización de bicosomas para la administración de antibióticos

Labiana SA

2011-2012

.....

Study of the "in vitro" Percutaneous Absorption of 6 compounds using pig skin samples

2013-2014

.....

Estudio mediante termogravimetría (TGA) de tres tejidos de poliéster con un corticoide incorporado

2013

.....

Lipid Peroxidation testing of two hair sets

2013

.....

Estudio comparative de la liberación "in vitro" de tres formulaciones conteniendo lidocaina y prilocaina. Fase II

2013

.....

Eficacia hidratante de un tejido de punto de poliamida

2013

.....

Apoyo tecnológico sobre el estudio comparativo de la liberación "in vitro" de cuatro formulaciones conteniendo lidocaína y prilocaína: fase i

2013

Moisture content of treated hair with tga

2013

UV actives for hair

2013-2015

Efecto antiarrugas de una formulación en la piel

2013

Apoyo tecnológico sobre el estudio de absorción percutánea in vitro de una formulación conteniendo naproxeno base

2012-2013

Apoyo tecnológico sobre el estudio de liberación "in vitro" de tres formulaciones conteniendo lidocaína y prilocaina

2012

Eficacia de la aplicación de polímeros con capacidad hidratante en piel humana

2012

Eficacia de cinco compuestos en piel humana

2012

Medición de la eficacia de los productos de dermofarmacia y cosmética solicitados por cinfa,

2012

In vivo and in vitro efficacy of single ingredients and finished products containing ceramides

2011- 2014

Trace - eficacia de antioxidantes en cabello humano

2009-2012

Research highlights

Development, stabilization and optimization of bicellar structures.

Phospholipids have an amphiphilic structure able to self assembly in aqueous solution. This capability allows the formation of a large number of nanostructures with different morphology and sizes, such as micelles, bicelles, bilayers, liposomes and bicosomes. Our group has a wide experience in the formation, characterization and dynamics of these aggregates. Bicelles are bilayered nano-aggregates formed by long and short chain phospholipid compounds dispersed in aqueous solution, which have proven to be interesting membrane-mimicking systems. These systems exhibit great morphological versatility depending on their composition and environment conditions such as hydration, temperature and pH, forming vesicles, discoidal structures, rolled-up aggregates, lamellar phases and more (Figure 1).

Figure 1: Cryo-TEM micrographs from different bicellar systems.

The discoidal aggregates have demonstrated a permeabilizing effect on membranes. This fact is very useful for dermatological applications. In the two last years, our group has optimized these nanostructures to be applied through different biological routes such as skin, mucosa and cerebrospinal fluid. Some of these substracts involve high water content. It is known that in diluted conditions, small discoidal bicelles became large structures and their properties are lost. The group has proposed several strategies to stabilize bicelles in dilute conditions in order to use these nanostructures in different applications. These strategies are based on encapsulation of bicelles into other lipid nanostructures, stabilization of the bicellar structures by use of polymers and stabilization using metallic nanoparticles.

Bicelles and bicosomes: new nanostructures for skin applications.

Bicosomes and bicelles are a new generation of nanostructures constituted by specific mixtures of phospholipids and other amphiphilic molecules with different alkyl chain length and degrees of unsaturation. These systems combine discoidal and vesicular structures, both of them based on lipid bilayers. Our results indicate that in topical applications, vesicle-shaped structures remain adhered to the skin surface being unable

to penetrate into the skin, probably due to their large and voluminous size. However, a proportion of the small discoidal structures have the ability to penetrate through the narrow intercellular spaces of the stratum corneum of the skin to reinforce its lipid lamellae. Thus, the different structures present in the system have different effects on the tissue. Bicelles and bicosomes are able to modify skin biophysical parameters and to modulate the skin's barrier function in vivo, acting to enhance drug penetration.

Additionally, these systems are able to incorporate drugs and molecules that can be carried through the skin layers. Encapsulation in bicelles and bicosomes provides advantages respect to incorporation in other carrier systems allowing the protection of the drug and increasing their efficacy.

The appropriate combination of different effects and the possibility to incorporate drugs offer a range of possibilities for these systems in development for skin care products.

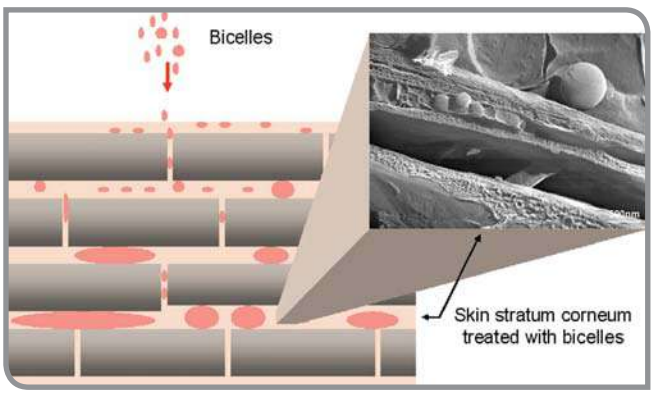


Figure 2: Representation of skin stratum corneum (SC) showing interaction with bicelles. Freeze-fracture electron microcopy image of SC treated with bicellar system.

Development of methodologies for lipokeratinic tissue characterization: X-ray scattering/Synchrotron, IR microespectroscopy/Synchrotron, electron microscopy, electron paramagnetic resonance (EPR).

In order to address studies on characterization of lipoqueratinic tissues such as skin, hair, mucosa, nails and more, the adaptation/optimization of high resolution techniques is needed. The group has wide expertise toward different microscopy techniques as freeze fracture electron microscopy (FFEM), freeze substitution electron microscopy (FSEM) and IR microspectroscopy using synchrotron radiation. These techniques are combined with small-angle X-ray scattering (SAXS) that provides information about the organization of lipids and proteins of the tissues. Recently and for the first time SAXS with transmission incidence using synchrotron radiation has been compared with grazing incidence with conventional X-ray source (GISAXS) in the study of the skin. Both methods provide the same type of information, but GISAXS is more sensitive to the surface and it is an ideal tool to characterize the structures in three dimensions.

Additionally, attenuated total reflectance-Fourier transform IR and EPR have reported about the vibrational characteristic frequencies of the alkyl chain lipids related to differently ordered phases of the lipokeratinic tissues and about the formation of free radicals in biological substracts.

Nano and microassemblies in the production of biofunctional textiles

Another research subject of our group is the production of biofunctional textiles and their effectiveness on skin properties. These textiles are able to release therapeutic compounds or cosmetics to the skin. The biofunctional textiles contain microscopic capsules of ingredients that break as the fabric rubs the skin, releasing the actives. Absorption and desorption behaviour of active agents embedded into the different biofunctional textiles should be taken into account when determining the amount of active agents incorporated into these textiles and when following the delivery mechanism as the fabric comes into contact with the skin. This group was working into this subject, preparing biofunctional textiles in order to know what exactly happen when textiles comes in contact with human skin, and to quantify the actives.

Microcapsules, microspheres, mixed micelles and liposomes were used as vehicles to be applied mainly in cotton and polyamide. Liposomes were prepared with wool lipid (IWL) extracts enriched with ceramides. Liposomes and microcapsules containing different active principles were applied on textile fabrics. As an active principle the ceramides present in the internal wool lipids have been used and as reference compounds caffeine and a sun filter (ethylhexyl methoxycinnamate) have been also used as tracers. Antioxidants such as resveratrol and gallic acid were also studied.

The demonstration of the active principle release by a close textile-skin contact, using a new specific design of percutaneous absorption was carried out (Figure 3).The passage of the active principle through different skin layers have been detected "in vitro". Most actives embedded within biofunctional textiles promoted an interesting reservoir effect.

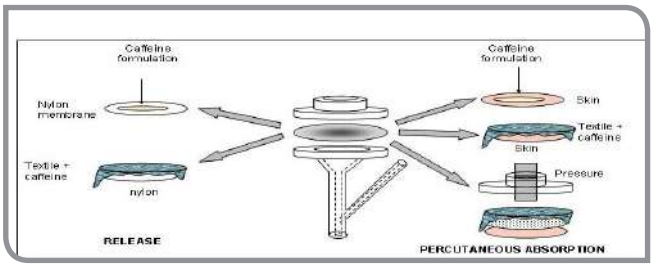


Figure 3: Design of percutaneous absorption: release by a close textile-skin contact

The passage of the active principle through the skin layers have also been detected "in vivo". In this research, textiles were applied onto volunteer forearms to determine their efficacy to the skin by non invasive techniques such as Tewameter and Corneometer as well as to detect the active compound in the stratum corneum by stripping method. From the results obtained, it has been demonstrated the effectiveness of an active compound encapsulated and applied onto a fabric when it is topically applied. IWL liposomes embedded in the biofunctional textile promote an increase of the level of skin hydration and a decrease of the TEWL values. On the other hand, the sun filter and gallic acid encapsulated were detected in the outermost layers of the stratum corneum.

Changes in the water properties of keratin fibers

This group also works into the cosmetic field, studying changes in the water properties of human keratin fibers, such as hair, nails, wool, stratum corneum from skin, etc. Reactive cosmetic treatments of hair, nails and skin, often impair fiber structure, resulting in an adverse effect on water absorption. The moisture absorption/desorption isotherm curves and the kinetics of these processes for hair, nail and skin are studied in this research. They behaved as expected, with a characteristic hysteresis between moisture uptake and desorption (Figure 4). The effect of lipid depletion on keratinized tissues, wool, hair and skin, were also followed by dynamic vapour sorption analyses. The general increase of the diffusion coefficients indicates the key role of the lipids in maintaining the adequate water permeability

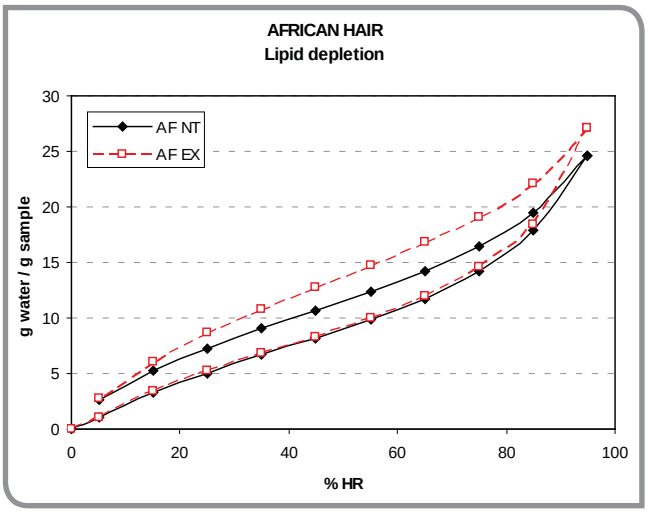


Figure 4. Absorption/desorption isotherm curves

The effects of different chemical cosmetic treatments on hair and skin are also evaluated by water absorption/desorption curves. Diffusion coefficients indicate the permeability of the fibre related to its integrity. Hair fibre damage has been also studied by surface morphology evaluation, shine measurements, differential scanning calorimetry, strength/relaxation etc. Special emphasis was devoted to photo damage determination of human hair and the antioxidants effect. Protein and tryptophan degradation, lipidic peroxidation and electron paramagnetic resonance were used to evaluate proteic and lipidic photodecomposition.

Summarizing, the main scientific activity from this Group is focus on the dermatological and textile application of lipid vehicles such as bicelles, liposomes, microspheres, etc., able to encapsulated active principles and favour its penetration in the different skin substrates. Percutaneous absorption profile is determined as well as its affectivity on hydration, barrier function, lipid peroxidation etc.

Collaborative leave at University of Regensburg

Functional materials

Our general research interests are centered in the development of functional materials with applications in areas such as biomedicine, catalysis, molecular sensing, coatings and adhesives, environmental remediation and energy. We believe that the discovery of new versatile and functional materials with solid prospect for practical applications will be intimately associated to inexpensive, simple and scalable processes. Thus, we aim to select the most practical chemical approaches for the synthesis of new materials and fine-tuning specific properties. In this sense, we like to apply in our projects what we call the "KISSu principle" (Keep It Simple and Sustainable). Besides materials synthesis, we maintain a genuine interest for the search of new synthetic methodologies and bioactive molecules (e.g., amidines, metal complexes).

STAFF

DAVID DIAZ DIAZ, GROUP LEADER
(UNIVERSITÄT REGENSBURG, GERMANY)

http://www-oc.chemie.uni-regensburg.de/diaz/index.php

PhD STUDENTS

Eva-Maria Schön
Dennis Kühbeck
Jürgen Bachl
Judith Mayr

MSc STUDENTS

Marleen Häring
Tobias Feldner
Judith Mayr

MSc STUDENTS

Marleen Häring
Tobias Feldner

Publications (articles)

Hydrolytic Conversion of a Metal-Organic Polyhedron into a Metal-Organic Framework

Mallick, A.; Garai, B.; Díaz, D. D.; Banerjee, R. *Angew. Chem. Int. Ed.* **2013**, 52, 13755-13759

Amino Acid-based Multiresponsive Low-Molecular-Weight Metallo-hydrogels with Load-bearing and Rapid Self-healing Ability

Saha, S.; Bachl, J.; Kundu, T.; Díaz, D. D.; Banerjee, R. *Chem. Commun.* **2014**, 50, 3004-3006

Dissolvable Metallohydrogels for Controlled Release: Evidence of a Kinetic Supramolecular Gel Phase Intermediate

Saha, S.; Bachl, J.; Kundu, T.; Díaz, D. D.; Banerjee, R. *Chem. Commun.* **2014**, 50, 7032-7035

Crossover Experiments Applied to Network Formation Reactions: Improved Strategies for Counting Elastically Inactive Molecular Defects in PEG Gels and Hyperbranched Polymers

Zhou, H.; Schön, E.-M.; Wang, M.; Glassman, M.; Liu, J.; Zhong, M.; Díaz, D. D.; Olsen, B. D.; Johnson, J. A. *J. Am. Chem. Soc.* **2014**, 136, 9464-9470

Research highlights

MULTISTIMULI RESPONSIVE SUPRAMOLECULAR GELS

The ability of natural systems to alter function in direct response to environmental conditions has inspired many scientists to fabricate 'smart' materials that respond to temperature, light, pH, electro/magnetic field, mechanical stress and/or chemical stimuli. These responses are usually manifested as remarkable changes from the molecular (e.g., conformational state, hierarchical order) to the macroscopic level (e.g., shape, surface properties). Among many types of stimuli responsive materials, self-assembled viscoelastic gels of both organic solvents (organogels) and water (hydrogels) have been recognized as promising materials for bottom-up nanofabrication tools in various fields such as biomedicine, catalysis, membranes, sensors, cosmetics, foods and environmental remediation. In contrast to chemical gels, which are based on covalent bonds (usually cross-linked polymers unable to redissolve), physical (also called supramolecular) gels are made of either low-molecular-weight compounds or polymers (gelators) through extensive non-covalent interactions.

Many gels have been found by serendipity rather than rational design, but we are also convinced that serendipity often provides a major opportunity for scientific discovery. We are interested in the development, modification, and applications of new multiresponsive and/or reactive supramolecular gels, including catalytic and self-healing metal-organic gels, as well as in the study of supramolecular chiral amplification with these materials. Herein, we try to find the most simple and reliable synthetic approaches for creating new and complex functions.

HYBRIDIZATION AND STUDY OF FUNCTIONAL POLYMER GELS

Many real-life applications of advanced materials such as SWCNTs are limited by two major problems: (1) their low dispersibility in aqueous solutions due to entanglement and hydrophobic association of the tubes; and (2) their intrinsic cytotoxicity. In this sense, significant progress has been made in the past few years regarding the surface functionalization of SWCNTs with various organic molecules to enhance both solubility and biocompatibility, and their blend with other systems to form composites with greater properties. Thus, the interest of incorporating CNTs into soft hydrogel matrices has grown considerably over the last decade. We envisioned the possibility of using the strain-promoted azide-alkyne cycloaddition (SPAAC) for covalent incorporation of SWCNTs into bioactive hydrogel networks. SPAAC has been proved to proceed efficiently not only in a wide range of conditions like the Cu(I)-catalyzed AAC, but also in the absence of ligands, bases or toxic metals. Thus, potential cytotoxic effects due to enduring entrapment of toxic metal ions especially in highly chelating gel matrices made by CuAAC could be overcome by SPAAC. We are interested in expanding the use of SPAAC and CuAAC to fabricate nanocomposites with tuneable properties such as conductivity, mechanical strength, and morphology, especially for biomedical and membrane applications such as targeted drug/gene delivery or tissue engineering.

In the broad field of polymer gels, we are also interested in the rational design of polymer gelators, including charged systems (e.g., polyelectrolytes), with enhanced gelation efficiency and new functionalities, for which we are employing molecular dynamic simulations with explicit solvent molecules in collaboration with Prof. C. Alemán (UPC).

FINE-TUNING THE BALANCE BETWEEN GELATION AND CRYSTALLIZATION

The formation of supramolecular gels is a result of a well-balanced combination of numerous non-covalent interactions, including those between gelator-gelator, gelator-solvent, aggregate-solvent and solvent-solvent molecules. Usually, a lack of control over these interactions caused an unpredictable competition between crystallization and gelation phenomena. We are learning about the key factors that govern the equilibrium position and how can we favor one of the two processes selectively in order to access to a wider range of materials with different properties from the same building blocks. In this sense, we couldsynthesize either metal-organic-frameworks (MOFs) or metal-organic-gels (MOGs) by small changes in the solvent composition using the same ligand and metal precursors.

CHEMICAL TRANSFORMATIONS IN CONFINED MEDIA

Inspired by nature, much effort has been devoted over the last decade to the study of meso-, micro- and nano-scale reactors. The main reason for this is the fact that many chemical reactions take place with high efficiency in natural confined environments where the motions of reactant molecules are restricted to that in free solution. In concordance, numerous advantages have been also attributed to the use of synthetic nanoreactors including, among others, the possibility of tailoring additional functionalities, organization and orientation of solvent, catalyst and reactant molecules, controllable molecular diffusion, large surface area to volume ratios and reduction of overheating/concentration effects. In our group we wish to understand the changes on kinetics and chemical pathways/selectivities of different types of reactions, including photochemical transformations, that are carried out within nanostructured and stimuli-responsive softgel materials, which can be tuned for working as reaction vessels, biocompatible nanoreactors and/or reusable catalysts. Beyond kinetics and selectivity aspects in comparison to solution phase, this project aims to contribute in building a challenge bridge between solution and biocompatible supramolecular responsive gel-based formulations for the selective activation and control release of bioactive compounds for the treatment of different diseases.

INTRINSIC CATALYTIC FUNCTION OF BIOPOLYMERS AND PROTEINS

With growing concern for our environment and stringent environmental regulations by the governments, emphasis of science and technology is shifting more and more from petrochemical-based feedstocks towards the optimal use of environmentally friendly and sustainable resources and processes. In this regard, direct utilization of products derived from naturally occurring materials has become a prevalent means for a number of high-tech applications. We found that many

natural polymers and proteins display an intrinsic ability for catalyzing important chemical transformations such as C-C bond forming reactions, which are in the broad sense a prerequisite for all life on earth.

The fact that natural materials can mediate these reactions under physiological conditions might have a significant impact on the evolution of different chemical compounds in vivo. Within our program we try to focus on these natural materials and understand the variables that can impact their inherent function towards different catalytic processes including cascade and multicomponent reactions. We believe that styding the intrinsic role of proteins in mediating bond formation/cleavage will be crucial for understanding mechanism in evolution and designing "greener" catalysts.

ADHESIVE POLYMERIC MATERIALS

Polymer chemistry has been a rich beneficiary of the ability of click reactions to make molecular connections with absolute fidelity. Polymer synthesis depends on a limited number of processes that include many of the best examples of click reactivity. During the last decade we have been working in collaboration with Prof. M.G. Finn (GaTech) in the development of new bulk polymers with adhesive properties for metal surfaces making use of the copper-catalyzed azide-alkyne cycloaddition. Some of our materials have been found to possess superior adhesive strength than standard commercial glues. We continue working on the improvement of these formulations as well as on the application of this technology in areas such as conductive materials, anti-fouling coatings, or superhydrophobic surfaces.

NANOPARTICLES-CONTAINING MATERIALS

In collaboration with the group of Dr. R. Banerjee (NCL), we participate on the preparation of highly stable metal and covalent organic framework-based materials (e.g., MOFs, COFs) with superior properties for applications in gas adsorption, catalysis, energy storage (e.g., water oxidation, hydrogen evolution), and biomedical applications (e.g., targeted anti-cancer drug delivery, diagnostic imaging). Moreover, we are interested in the development of new physical and chemical strategies to stabilize unstable nanoparticles, and on the use of functional nanoparticles to stabilize other structured materials.

Facilities

IQAC Facilities

- Custom Antibody Service (CAbS)
- Characterization of Colloidal Dispersion Service
- Microanalysis Service
- Biodegradation and Aquatic Toxicity Service
- Skin Absorption and Skin Efficacy Services
- Synthesis of High Added Value Molecules Service
- Proteomics Service
- Thermal Analysis Service
- SAXS-WAXS Service
- Magnetic Resonance Service
- Lipidomics and UPLC-TOF
- Knowledge Transfer

Custom Antibody Service

The CAbS is a joint facility established under the umbrella of the IQAC-CSIC and CIBER-BBN. The facility wants to offer a high quality service for customized monoclonal and polyclonal antibody production against many types of antigens including proteins, peptides or small organic molecules. Moreover, CAbS can offer additional services related to the preparation of immunoreagents and development of immunochemical methods and protocols.

STAFF

Mª PILAR MARCO COLÁS (SUPERVISING SCIENTIST)
NURIA PASCUAL DURAN (TECHNICAL DIRECTOR)
MARTA RUIZ ARRIBAS
ANA GONZÁLEZ GONZÁLEZ

Detailed description of the services and features provided by CAbS

A) Monoclonal Antibody Development

The standard service includes:

1. Discussion of the project (screening system, selection criteria, etc.) and planning the work.

2. Immunization, cell fusion, screening and cloning: After their fusion with myeloma cells screening of the best hybridomas will be performed by ELISA using previously supplied antigen. Specific clones will be subcloned by limiting dilution.

3. The customer will receive two cryovials and 10 ml of culture supernatant of each positive clone.

B) POLYCLONAL ANTIBODY DEVELOPMENT

The standard service includes:

1. Discussion of the details of the project including features such as the type of immunogen, the final properties of the antibodies, and the species and number of animals used.

2. Immunization protocol: As accorded by the customer.

3. Isolation of the antiserum

4. ELISA testing: samples obtained on each boosting injection and the final antisera will be tested against the antigen following the criteria agreed upon in the previous discussion with the costumer. The costumer will receive 60-80 mL of the final serum from each rabbit and about 5 mL samples of the pre-immune serum, and the blood extractions made during the immunization protocol after each boosting injection.

C) ADDITIONAL SERVICES:

1. Preparation of bioconjugates: labeled antibodies, haptenized proteins and enzymes, biotynilated and fluorescent probes, gold nanoparticle conjugates, etc.

2. Antibody purification.

3. Development of immunochemical methods: ELISA, immunoaffinity columns, etc.

4. Antibody characterization (Isotyping).

5. Hybridoma cryopreservation.

6. Mycoplasma testing

Unless otherwise stated in a signed agreement, the property of immuno (bio) reagents produced or synthesized and the results obtained regarding establishment of immunochemical methods and procedures will belong to the costumer

Characterization of Colloidal Dispersions Service

This service deals with the characterization of nano-structured liquids (e.g. micelles, vesicles, liquid crystals, microemulsions, nano-emulsions etc.) and solid dispersions (e.g. organic inorganic or hybrid nanoparticle suspensions).

The characterization implies determination of size, morphology, phase transitions, surface, interfacial and rheological properties.

The service responsible group is member of TECNIO (ACC1Ó) and has been awarded with a quality certificate (similar to ISO 9001) by ACC1Ó (Generalitat de Catalunya).

SUPERVISING SCIENTISTS

NURIA AZEMAR SAZATORNIL
CONXITA SOLANS MARSÀ

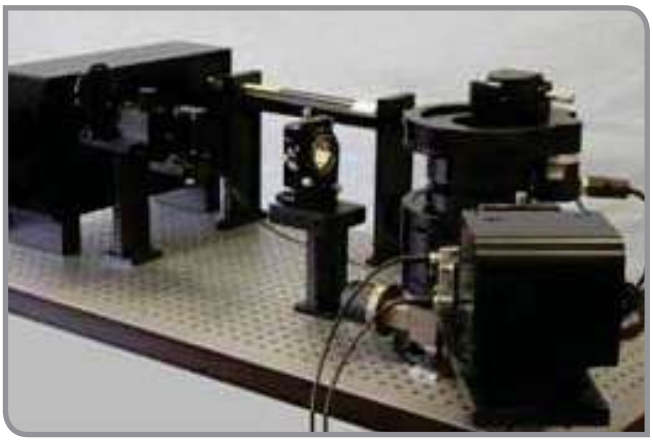
TECHNICAL ASSISTANT

SUSANA VILCHEZ MALDONADO

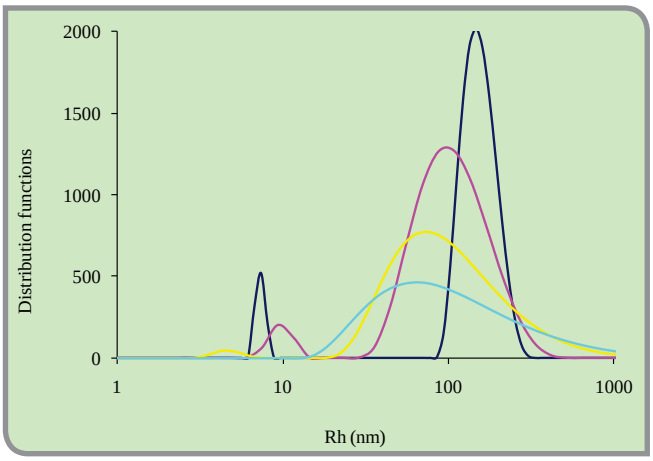
Relevant techniques:

Static (SLS) and dynamic (DLS) light scattering

Determination of particle size distribution, shape, diffusion coefficient, aggregation number, molecular weight of colloidal dispersions



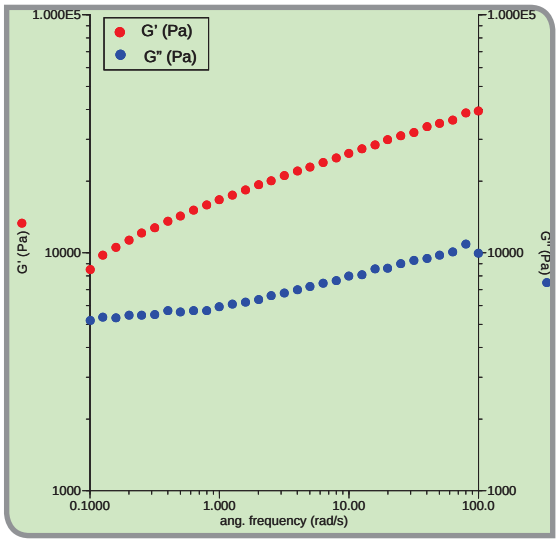
3DDLS Spectrometer



Size distributions of mixed micelle and vesicle dispersions by dynamic light scattering

Rheology

Determination of rheological properties of fluids and soft matter in flow and deformation regimes by steady state (viscosity, shear thinning, shear thickening) and dynamic (elastic and viscous moduli, relaxation time) measurements

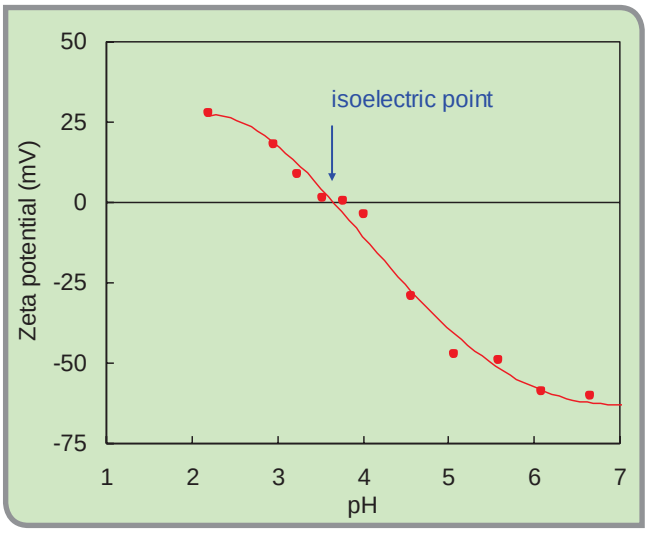


Rheometer AR-G2

Variation of elastic (G') and viscous (G") moduli as a function of frequency

Electrophoretic mobility

Determination of Zeta potential of charged particles

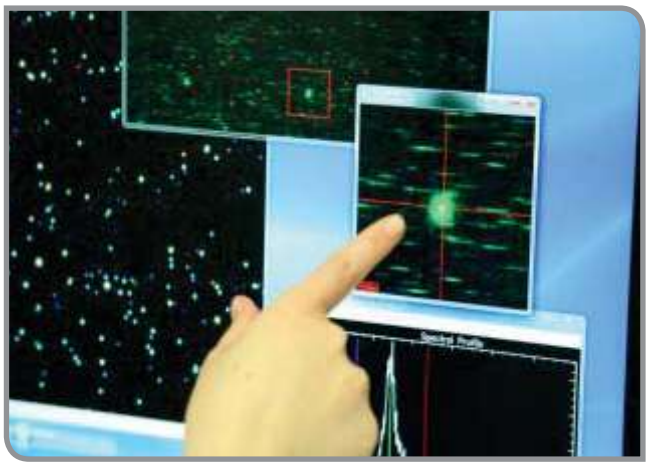


Zetasizer Nano Z

Variation of Zeta potential as a function of pH

High resolution optical microscopy with spectral analysis

This technique allows to visualize nanosize objects (e.g. nanoparticles, nano-emulsions) and to determine the light spectra of the sample analyzed.



Other techniques:

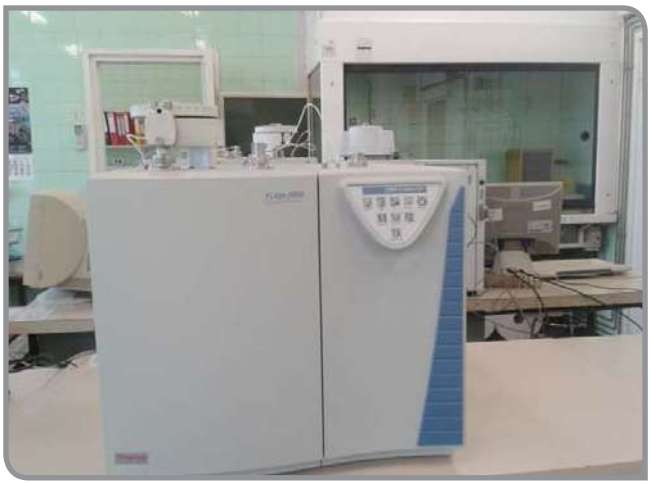
- Laser Light Diffraction
- Light back scattering
- Differential Refractometry
- Tensiometry
- Optical Microscopy

Microanalysis Service

The Microanalysis Service provides micro-determination of total carbon, hydrogen, nitrogen, sulphur (C, H, N, S) and halogens present in a wide range of organic and inorganic compounds.

Since March 1999, Microanalysis Service has been accredited by ENAC, under EN45001 regulation. This was the first accredited elemental microanalysis by the CSIC and the first to be accredited in Spain

As of November 2001, this Service has been accredited under regulation UNE-EN ISO/IEC 17025 for analysis of CHNS until at the end of November 2012.



STAFF

MARIA TERESA VILA TERRADES (Contacting person)
NURIA BARRERA DE PAZ

EQUIPMENT

This facility has the appropriate instruments for accurate sample analysis. Primary Instruments:

1 Elemental Microanalyzer (A5) model Flash 1112, for C,H,N determination.

1 Elemental Microanalyzer (A4) model Flash 2000, for C,H,N,S determination.

2 Mettler Microscale (B3 and B4) models MT5 and MX5.

1 Metrohm Titrando model 808 for Cl,Br,I and F determination.

Biodegradation and Aquatic Toxicity Service

The Biodegradation and Aquatic Toxicity Service of the IQAC offers a full range of standardized test methods (OECD technical guidelines) for the assessment of the biodegradability and toxicity of organic compounds in the aquatic environment.

This service carries out biodegradation and aquatic toxicity tests for internal use and for external clients from industry, public administration, universities, and research organisms. Suitable technology and an expert and qualified staff guarantee the availability of results.

STAFF

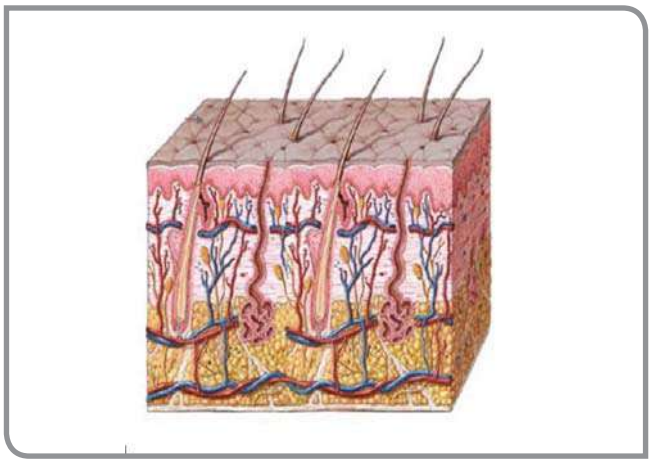
MARÍA TERESA GARCÍA RAMÓN (Contacting person)
ISABEL RIBOSA FORNOVI
FRANCESC COMELLES FOLCH
ISABEL MUÑOZ LIRÓN
ROSA MARÍA SALVIA PEIRÓ

Skin Absorption Service

The Microanalysis Service provides micro-determinaThe Skin Absorption Service deals with the knowledge and quantitation of the skin absorption of a given compound applied topically. Using an in vitro methodology officially accepted by the OCDE (2004), the distribution of a chemical in the different skin compartments (stratum corneum, epidermis and dermis) can be detected and quantified. The studies of percutaneous absorption can be fundamentally of interest for the Pharmaceutical, Cosmetic, Veterinary and Chemical sectors.

STAFF

JOSÉ LUIS PARRA JUEZ (Supervising scientist, Contacting person)
CRISTINA ALONSO MERINO
LAIA RUBIO TOLEDANO



Skin Efficacy Service

The Skin Efficacy Service deals with the experimental design, evaluation and objective diagnostic of the skin efficacy and tolerance of cosmetic and dermatologic formulations topically applied by the use of non-invasive biophysical techniques. Evaluation and diagnosis of other keratinized tissues such as human nails and hair.

STAFF

LUISA CODERCH NEGRA (Supervising scientist, Contacting person)
CLARA BARBA ALBANELL
ISABEL YUSTE HERNÁNDEZ

Synthesis of High Added Value Molecules Service

SIMchem (service of Synthesis of High added value Molecules) is a IQAC-CSIC research facility created in 2009 to give chemical and synthetic support to (R+D+i) activities in industry, university and public organizations.

It is projected to fill the gap existing between custom synthesis performed by companies and the synthetic research groups in academy. The service is intended to give a synthetic support to research projects of chemistry, biology, biomedicine and drug discovery by providing both skilled personnel, instrumental and laboratory, and taking advantage of the chemical and synthetic expertise of the different groups present in the Institute.

The service will be devoted to the study of synthetic methodologies, the development of synthetic sequences and small scale synthesis of high added value organic compounds (milligram to gram). The type of compounds initially envisaged consist in broad scope bioactive molecules, including drug candidates, pharmacological tools and molecules directed to chemical, biological or biophysical tests in R+D activities.

Another goal of the service is to implement new efficient synthetic technologies in the host Institute, which could be employed by the research groups present in the IQAC, or external users. A special effort will be devoted to set up high safety methods of synthesis that could improve current laboratory practices in the Institute and reach a high level of competence and efficiency. SIMchem plans to reach the state-of-the-art in synthetic and preparative purification technologies that, in general, wouldn't be available to individual groups in the IQAC.

LINES OF EXPERTISE

Medicinal chemistry.
Heterocyclic and condensation chemistry, multistage synthesis.
Development and optimization of reactions and processes.
Analytical support to organic synthesis.

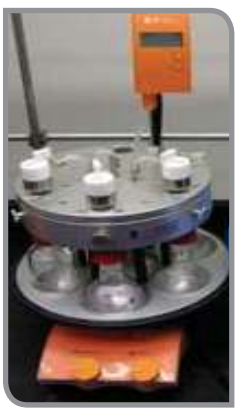
CONTACTS

AMADEU LLEBARIA, PhD
Tel. (+34) 93 400 61 00 Ext. 1214
amadeu.llebaria@cid.csic.es

CARME SERRA, PhD
Tel. (+34) 93 400 61 00 Ext. 1217
cscsim@cid.csic.es

INSTRUMENTAL TECHNOLOGIES

SYNTHESIS



Carousel reaction station.

Parallel synthesis station for solution phase chemistry and solid supported reagent based synthesis

Simultaneously heats/cools, stirs and reflux´s multiple samples under an inert atmosphere

Hydrogenation chamber

OTHER INSTRUMENTS and FACILITIES

Systems for samples evaporation: Thermo Fischer SpeedVac and Stuart Sample Concentrator.
Karl Fisher analysis.
Hydrogenation Lab (microscale, low pressure).
Mass spectrometry

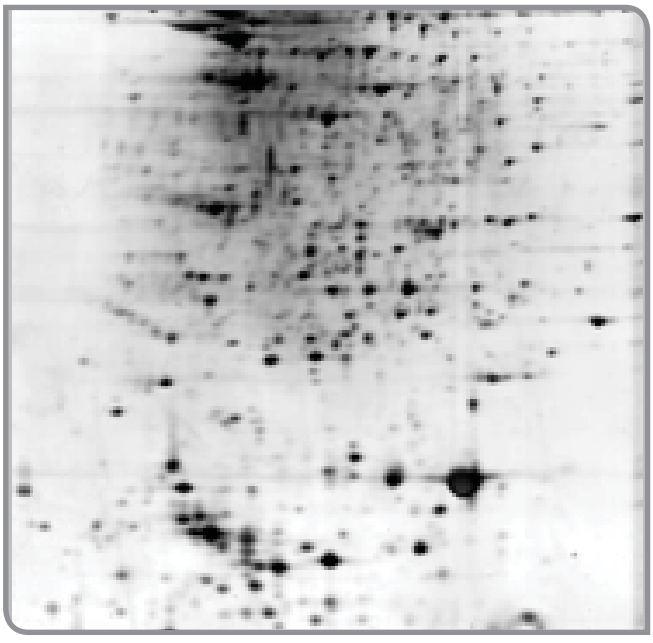
ANALYTICAL AND PURIFICATION TECHNIQUES

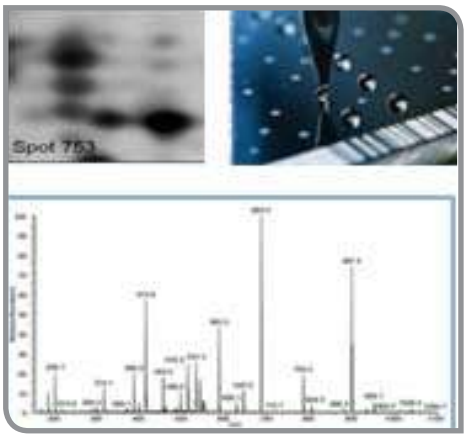
Analytical and preparative HPLC.
Automated flash and MPLC chromatography.

Proteomics Service

The Proteomics Service has been recently created to provide support to IQAC and IDAEA researchers as well as other public and private organizations. The service is focused in the analysis of biomolecules (proteins, peptides, oligonucleotides, sugars ...) and large organic molecules (such as polymers, dendrimers, polyphenols and other macromolecules) by MALDI-TOF/TOF mass spectrometry.

The Service also offers separation, quantification, identification and characterization of peptides and proteins in biological and biomedical systems using two-dimensional electrophoresis and mass spectrometry techniques.





STAFF

CARME QUERO LÓPEZ
(Supervising scientist, Contacting person)

SERVICES

- Molecular mass determination by MALDI-TOF mass spectrometry.
- Identification of proteins by peptide mass fingerprint.
- Identification of proteins by peptide mass fingerprint and peptide fragmentation by mass spectrometry (MALDI-TOF/TOF).
- Electrophoresis Separation of proteins by one- and two-dimensional electrophoresis.

Thermal Analysis Service

TAS was formally founded in 1999, in order to meet the growing needs in this field of existing research groups, currently in IQAC, and collaborate in the process of innovation and industrial development.

The following techniques are available:

- Differential scanning calorimetry DSC
- Microdifferential scanning calorimetry
- Thermogravimetric analysis TGA
- Dynamic vapor sorption DVS
- Thermomechanical analysis TMA

STAFF

ALBERT M. MANICH BOU (Supervising scientist)
JOSEP CARILLA AUGET (Contacting person)

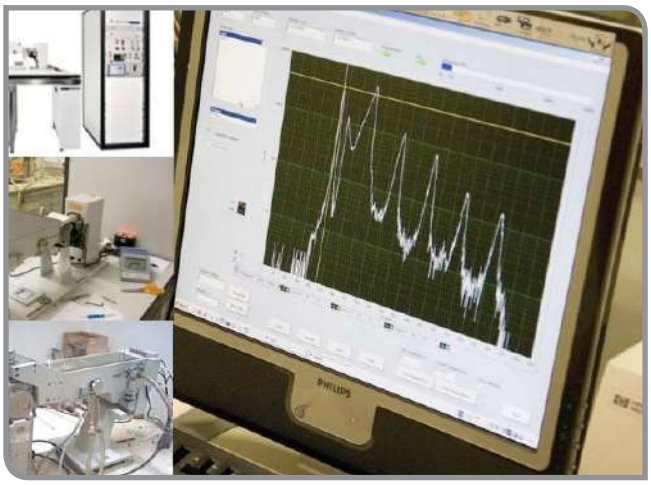
SAXS-WAXS Service

The SAXS-WAXS service provides measurements with a variety of set ups for the determination of structural information of ordered and semi-ordered materials. The

range of distances of interest falls in the nanoscale domain (0.2-100 nm). It can allow determinations of size, space ordering, morphology, fractal dimension and total interfacial area. The materials comprise surfactant solutions and liquid crystals, mesoporous materials, macromolecules in solution such as proteins or DNA, nanostructured films and any conceivable material with electronic discontinuities in the above mentioned range. 1D and 2D detectors are available. GISAXS and GIWAXS configurations are also possible.

STAFF

RAMON PONS PONS
(Supervising scientist, Contacting person)
JORDI ESQUENA MORET
(Supervising scientist, Contacting person)
JAUME CAELLES BALCELLS



Magnetic Resonance Service

The Magnetic Resonance Service is a research support facility for the IQAC, other universities and public research organisms, as well as for private companies. To two types of spectroscopy techniques are available:

Nuclear Magnetic Resonance (NMR Unit):

The Unit provides access to the following state-of-the-art methodologies:

- Structure elucidation and quality control in synthetic chemistry by solution 1D/2D-NMR.
- NMR-based drug screening.
- NMR of cells, cell extracts, and metabolomics-by-NMR.
- Diffusion experiments and DOSY.

Electronic Paramagnetic Resonance (EPR Unit):

The electron paramagnetic resonance spectroscopy (EPR) or electron spin resonance (ESR) studies the interaction of a paramagnetic species with the electromagnetic radiation (microwave radiation) in the presence of an external magnetic field and allows detecting and studying stable or transient paramagnetic species such as free radicals, some transition metal ions and defects in materials.

STAFF

YOLANDA PÉREZ RUIZ (NMR UNIT MANAGER)
LLUÍS FAJARÍ AGUDO (EPR UNIT TECHNICAL MANAGER)
LLUÍS JULIÀ BARGÉS (EPR UNIT SCIENTIFIC MANAGER)

TECHNICAL ASSISTANTS

AVENCIA DIEZ ORTEGO

Nuclear Magnetic Resonance Unit (NMR Unit)

The NMR Unit has two Varian/Agilent Spectrometers:

Varian Mercury 400 MHz (9.3950 T) is the walk-up instrument for automated heteronuclear NMR.

The spectrometer has a VNMRS console with Direct Digital receiver with Performa-I Z gradients and OneNMR probe, which can be tuned automatically to any nucleus between ^{15}N and ^{31}P with ProTune System autotuning and is using Agilent's Chempack pulse sequences suitable for most routine measurements. This spectrometer delivers routine, rapid heteronuclear-detected spectra in automation (^{1}H, ^{19}F, ^{31}P, ^{13}C, ^{11}B, ^{15}N, ^{29}Si, ^{2}H, ^{17}O, ^{111}Cd, ^{113}Cd, ^{105}Pd, ^{77}Se, ^{27}Al, ^{119}Sn and ^{195}Pt). An automated 100-sample changer (for standard 8" long/5 mm Ø NMR tubes) and VnmrJ3.2 software allow performing short acquisitions and quick access to spectra during the daytime hours (9 am to 7 pm), while longer experiments such as 2D HSQC or HMBC are submitted to run overnight or week-ends.

Varian Inova 500 MHz (11.7440 T field strength) is used for kinetics, diffusion, drug discovery and variable temperature experiments (besides standard experiments).

The spectrometer is equipped with a two-channel Inova console, Performa-II (60 G/cm) Z gradients, and an inverse detection AutoX probe. Is the instrument of choice for more demanding samples, and is frequently used for the full characterization of samples where tiny amounts of material are available. The 500 is using DOSY/Biopack pulse sequences and VnmrJ software 2.2D version.

Electronic Paramagnetic Resonance (EPR Unit)

Equipped with a Bruker EPR/ESR spectrometer EMX, with a microwave bridge of X-band (~9 GHz) EMX premium X, magnet of 10" ER073 with a power supply of 12 KW ER083.

The following accessories are available: Standard or double cavity; different container samples (quartz tubes, quartz capillaries,cells, flat cells for tissue); liquid nitrogen dewar and variable temperature accessory: cryostat, liquid nitrogen transfer line (120 K – 373 K); intelligent temperature controler ITC 503S from Oxford Instruments; continuous flow cryostat system of liquid helium (4.2 K - 300 K); gas flow controller from Oxford Instruments; high vacuum unit HP40B2 from Vacuubrand; "in situ" radiation source of UV-vis. 500 W Oriel pressure mercury lamp. Power supply Newport 69910; Bruker software acquisition, processing and simulation spectra WINEPR and SimFonia.

Lipidomics Core Facility

The Lipidomics Core Facility conducts comprehensive analysis of cellular lipids that encompass fatty acyls, glycerolipids, glycerophospholipids and sphingolipids. Such studies are possible with the advent of sophisticated mass spectrometric techniques. The services include sample preparation, lipid identification by mass spectrometry, LC-MS lipid profiling, LC-MS lipid quantification, and training in sample preparation methods.

STAFF

JOSEFINA CASAS (Supervising Scientist)
EVA DALMAU (Technician)

SERVICES

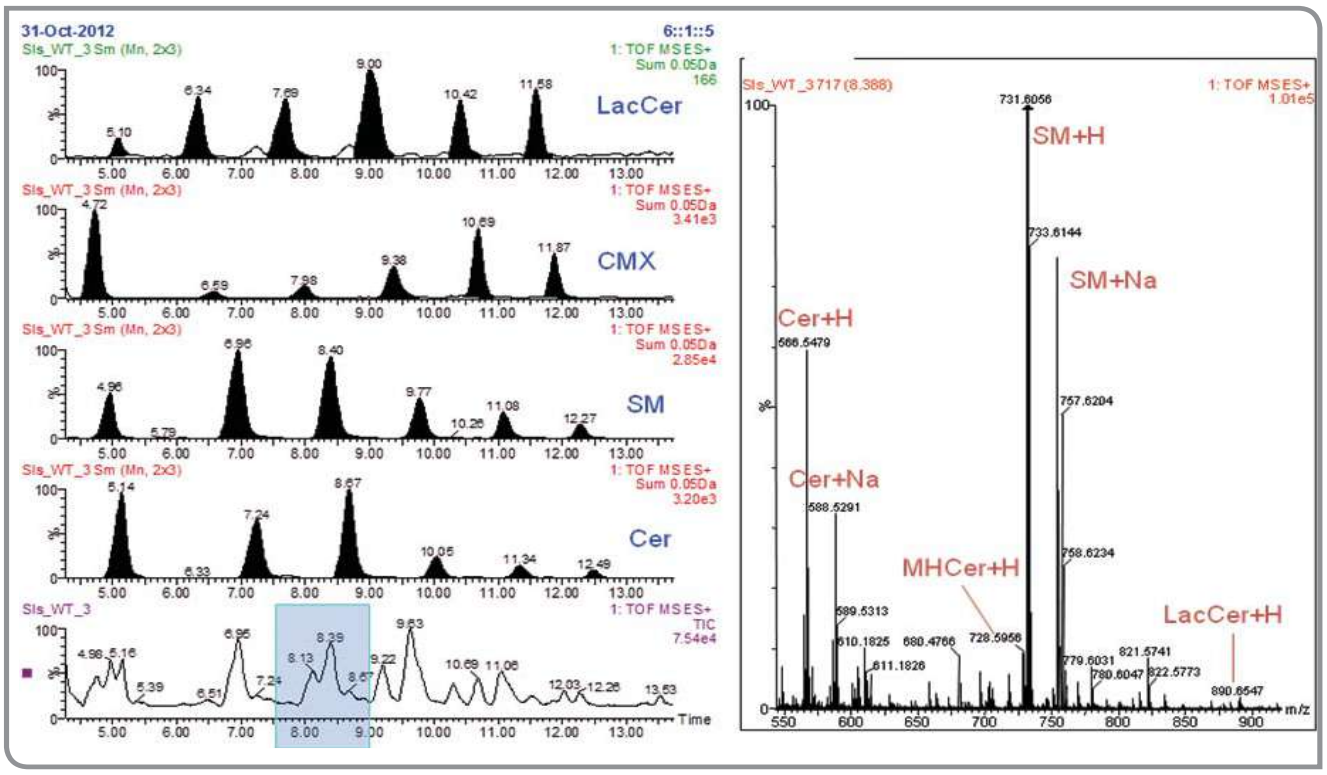
Determination of the sphingolipid composition.

Addition of internal standards, extraction, purification and analysis by UPLC-TOF. Compounds are identified by its retention time and exact mass. The identification and quantification of sphingosine, sphinganine, sphingosine-1-phosphate and sphinganine-1-phosphate is carried out by HPLC-MS/ MS.

Class of compounds: Sphingosine and dihydrosphingosine, sphingosine-1-phosphate and sphinganine-1-phosphate, ceramide and dihydroceramide, sphingomyelin and dihydrosphingomyelin, hexosylceramide (glucosyl- and galactosyl-ceramide), lactosylceramide and dihydrolactosylceramide. Identification and relative amount of ganglioside molecular species.

Determination of the glycerolipid and glycerophospholipid composition.

Addition of internal standards, extraction, purification and analysis by UPLC-TOF. Compounds are identified by its retention time and exact mass. Available internal standards: triacylglicerol, diacylglycoreol, monoacylglicerol, phosphatidylcholine, plasmalogen, lysophosphatidylcholine, lysoplasmalogen, phosphatidylserine, lysophosphatidylserine, phosphatidylethanolamine, lysophosphatidylethanolamine. The number of carbon atoms and double bonds of the acyl groups will be indicated, but not it localization. It is possible to detect and quantify cholesteryl esters.



Knowledge Transfer

Knowledge Transfer encompasses the systems and processes by which technology, expertise and skilled people are transferred from the research environment (universities, centers and institutes) to the industry, commerce and public sectors to contribute to prosperity and society's benefit.

In the knowledge transfer process, we interact with researchers to identify and evaluate the technologies with potential commercial interest, adequately protect such technologies by means of patents, etc, and develop strategies to final negotiation and transfer to the companies who can exploit the final technology.

STAFF

ISABEL MASIP Ph.D
Knowledge Transfer Manager
Deputy Vice-Presidency for Knowledge Transfer

TECHNOLOGIES AVAILABLE

We have available a wide range of technologies in human health, diagnostic tools, cosmetics, chemical devices, etc. and the know-how acquired by our researchers in different technological fields.

Different collaborative approaches are offered, such as exclusive and non-exclusive patent licenses, and collaborative research and contract research with industry based on patent licences or in innovative technologies.

LIFE SCIENCES

Cancer

IQAC_006. Aminocyclitol derivatives to regulate immune response by stimulation of natural killer T-cells.
IQAC_018. Ceramide analogues as potential anti-tumour drugs.

Inflammatory diseases

IQAC_009. Modified siRNAs for silencing TNF-α gene expression to treat inflammatory diseases.
IQAC_011. New siRNAs conjugated to hydrophobic molecules for silencing gene expression in the treatment of inflammatory diseases.
IQAC_012. Optimization of the therapeutic potential of siRNA by formation of complexes with plasma components.

Rare diseases

IQAC_008. New aminocyclitols for treatment of Gaucher disease.
IQAC_013. New compounds for treatment of Gaucher disease.

Immunology/adjuvants

IQAC_006. Aminocyclitol derivatives to regulate immune response by stimulation of natural killer T-cells.

Pain

IQAC_022. Pain treatment based on TRPV1 channel blockers.

Eating disorders

IQAC_021. Treatment of diseases related to eating disorders.

CNS

IQAC_049. Optopharmacological compounds targeting mGlu5 receptors.
IQAC_042. Treatment of diseases and degenerative processes caused by apoptosis

Medical diagnosis

IQAC_002. Test for cancer diagnosis based in the quantification of acid ceramidase.
IQAC_019. Test for early diagnosis of rheumatoid arthritis based on chimeric fibrin and filaggrin peptides.
IQAC_020. Test for early diagnosis of rheumatoid arthritis based on chimeric vimentin peptides.
IQAC_041. Immunoassay to detect residual doxycycline in food.
IQAC_043. Immunoassay for rapid detection of oral anticoagulants in blood.
IQAC_047. Immunoassay for rapid diagnosis of infectious diseases caused by *Pseudomonas aeruginosa.*

Drug delivery

IQAC_007. Bicosomes: bicelles encapsulated in liposomes and their application in diluted systems.

CHEMICAL TECHNOLOGY

Characterisation Devices

IQAC_023. Kratky type X-ray scattering cameras modified to work under controlled atmosphere conditions.

Annexes

LIST OF PERSONNEL

SCIENTIFIC STAFF

Abad Saiz, José Luis	Científico Titular
Alfonso Rodríguez, Ignacio	Científico Titular
Anglada Rull, Josep Maria	Investigador Científico
Arsequell Ruiz, Gemma	Investigador Científico
Azemar Sazatornil, Núria	Investigador OPIS
Blanco Fernández, Jerónimo	Investigador Científico
Bosch Verderol, Pilar	Científico Titular
Bujons Vilas, Jordi	Científico Titular
Caminal Saperas, Glòria	Investigador Científico
Casas Brugulat, Josefina	Investigador Científico
Clapés Saborit, Pere	Profesor de Investigación
Coderch Negra, Luisa	Profesor de Investigación
Coll Toledano, Josep	Profesor de Investigación
Comelles Folch, Francesc	Científico Titular
Cot Cosp, Jaume	Profesor de Investigación
Crehuet Simón, Ramon	Científico Titular
Delgado Cirilo, Antonio	Profesor de Universidad
Díaz Díaz, David	Científico Titular
Eritja Casadellà, Ramon	Profesor de Investigación
Esquena Moret, Jordi	Científico Titular
Fabriàs Domingo, Gemma	Profesor de Investigación
Galve Bosch, Roger	Científico Titular
García Ramon, Mª Teresa	Científico Titular
Gomara Elena, Mª José	Científico Titular
Guerrero Pérez, Angel	Profesor de Investigación
Haro Villar, Isabel	Investigador Científico
Infante Martínez-Pardo, Mª Rosa	Profesor de Investigación
Joglar Tamargo, Jesús	Científico Titular
Julià Bargés, Lluís	Investigador Científico
Llebaria Soldevila, Amadeu	Investigador Científico
López Serrano, Olga	Investigador Científico
Maldonado, Fernando	Científico Titular
Manich Bou, Albert Mª	Investigador Científico
Marco Colás, Mª Pilar	Profesor de Investigación
Marsal Monge, Agustí	Investigador Científico
Maza Ribera, Alfonso de la	Profesor de Investigación
Messeguer Peypoch, Àngel	Profesor de Investigación
Molina Mansilla, Ricardo	Científico Titular
Olivella, Santiago	Profesor de Investigación
Parra Juez, José Luis	Profesor de Investigación
Pérez Muñoz, Lourdes	Científico Titular
Pinazo Gassol, Aurora	Científico Titular
Pons Pons, Ramon	Investigador Científico
Reig Isart, Francisca	Profesor de Investigación
Rosell Pellisé, Gloria	Profesor de Universidad
Sánchez Baeza, Francisco	Profesor de Investigación
Solans Marsà, Conxita	Profesor de Investigación
Torres Simó, Josep Lluis	Profesor de Investigación
Triola, Gemma	Científico Titular
Valencia Parera, Gregori	Investigador Científico

TECHNICAL STAFF

Barrera de Paz, Nuria	Ayudante de Investigación
Bleda Hernández, Mª José	Titulado técnico
Carrera Altarriba, Imma	Auxiliar de Investigación
Caelles Balcells, Jaume	Técnico Especializado de OPIS
Carilla Auguet, José	Técnico Especializado de OPIS
Díez Ortego, Avencia	Ayudante de Investigación
Fajarí Agudo, Luis	Técnico Superior Especializado
Ferrero Virgos, Carmen	Ayudante de Investigación
González Chaparro, Juan José	Ayudante de Investigación
Lloria Tolrà, Juan	Técnico Especializado de OPIS
Martí Gelabert, Meritxell	Ayudante de Investigación
Muñoz Lirón, Isabel	Ayudante de Investigación
Nogués Gorri, Emilio	Ayudante de Investigación
Pascual Durán, Nuria	Téc. Sup. Especializado de OPIS
Pérez Ruiz, Yolanda	Téc. Sup. Especializado de OPIS
Salvia Peiró, Rosa Maria	Ayudante de Investigación
Sindreu Grañé, Montserrat	Ayudante de Investigación
Vila Terrades, Mª Teresa	Técnico Especializado de OPIS
Vilchez Fernández, Amalia	Ayudante de Investigación
Yuste Hernández, Isabel	Ayudante de Investigación

ADMINISTRATION STAFF

Beltrán Fabregat, Lídia	Auxiliar de Administración
Moliner Ferrer, Leonor	Auxiliar de Administración

POSTDOCTORAL FELLOWS

ALAM, MOHAHMAD MYDUL
ALEJANDRO VÍLCHEZ VILLALBA, ALEJANDRO
ALONSO MERINO, CRISTINA
AUBERY TORRES, CAROLINA
AVIÑÓ ANDRÉS, ANNA MARIA
BARBA ALBANELL, CLARA
BARBOSA-BARROS, LUCYANNA
BEDIA GIRBÉS, CARMEN
BOSCH HEREU, LLUÍS
BURGUETE PEREZ , ASUNCIÓN
CALDERÓ LINNHOFF, GABRIELA
CARRASCO ROMERO, ESTHER
CÓCERA NÚÑEZ, MERCEDES
CONTANT, SHEILA
CORREDOR, MIRIAM
DOLS, AURORA
FÀBREGA CLAVERÍA, MARIA CARME
FAGGI, ENRICO
FERNANDEZ VILA, OLAIA
FIGUERA, NATALIA DE LA
GARCIA FERNANDEZ, LORENA
GARRIDO LOPEZ, CRISTINA
GARRIDO, MARÍA
GRIJALVO TORRIJO, SANTIAGO
GUERRA REBOLLO, MARTA
YOUSSEF HARRAK, YOUSSEF
JIMENO MOLLET, CIRIL
LOPEZ ROMERO, SERGIO
MARTÍNEZ RODRÍGUEZ, MARÍA
MEZEI, AMALIA
MORROS CAMPS, JORDI
MUÑOZ RUBIO, LOURDES
NESTOR, JEREMIE
PATTI, ALESSANDRO
PÉREZ JIMÉNEZ, JARA
PÉREZ RENTERO, SONIA
QUERO LÓPEZ, CARMEN
RAMOS MACIAS, VICTORIA ELENA
RAMOS ROMERO, SARA
RODRÍGUEZ DELGADO, GELEN
RODRÍGUEZ NÚÑEZ, MONTSERRAT
RUA, FEDERICO
RUBIO TOLEDANO, LAIA
RUBIO VIDAL, NURIA
SALVADOR VICO, J.PABLO
SERRA, CARME
SINGH, MANROSHAN
SOLA OLLER, JORDI
SOLÈ FONT, ISABEL
TAVANO, LORENA
TERRAZAS MARTÍNEZ, MONTSERRAT
TORRENT SUCARRAT, MIQUEL
VALDIVIELSO PABLO, ANGEL MANUEL
VALERA CANO, ENRIQUE
VÁZQUEZ, ANA
VILCHEZ MALDONADO, SILVIA
VÍLCHEZ MALDONADO, SUSANA

Ph. D. AND MASTER STUDENTS

ALAGIA, ADELE
ALCAIDE, ANNA
ALMEIDA COTRIM, BRUNO
ATCHER UBIERGO, JOAN
BABINGTON, RUTH
BAUTISTA PÉREZ, MARÍA ELENA
BORRÀS, ROSER
BROTO AVILES, MARTA
BURGOS MÁRMOL, JOSÉ JAVIER
BUSTELO, MARTA
CALAFELL, EMELINE
CALDERON ALMENDRO, RAQUEL
CARCILLO, MAGALIE
CARRERAS CARDONA, ANNA
CASASAMPERE, MIREIA
COLOM SANMARTÍ, GLORIA
CUADROS DOMÉNECH, CUADROS
CINGOLANI, FRANCESCA
COLOMER COLL, MERITXELL
CONCIA, ALDA LISA
FERNANDEZ ARAUZO , LETICIA
FERNÁNDEZ PINTO, ESTIBALIZ
FERREIRA, RUBEN
FONT, JOAN
FORNAGUERA, CRISTINA
FURSTENAU, BEN
GAGO OTERO, RAFAEL
GALATOLA, RAMONA
GARCIA FEBRERO, RAUL
GARRABOU PI, XAVIER
GÓMEZ CORTÉS, LIVIA
GOMEZ-SANTACANA, XAVIER
GONZÁLEZ PINACHO, DANIEL
GUNLER, INCI
GUTIERREZ TEJEDA, MARIANA
HERNANDEZ ALBORS, ALEX
HERNANDEZ SANCHEZ, KAREL
HOMS SAN MILLÁN, MARIA
KOTRONOULAS, ARISTOTELIS
LAFUENTE FABRA, MARIA
LEITNER, STEFANIE
LENDÍNEZ GRIS, MARIA DEL CARMEN
LLINÀS PONS, MERITXELL
MAGAÑA RODRIGUEZ, RODRIGO
MARCOS BENTEO, ENRIQUE
MARTÍNEZ RODRÍGUEZ, MARIA
MATAS MOYA, SÓNIA
MESA, JOSÉ ANTONIO
MIRAS HERNÁNDEZ, JONATHAN
MOLINAR, EUNICE
MONLLEÓ, ESTER
MURIANO CASTAÑÓN, ALEJANDRO
NAVARRO MOSLAN, DIANA
NIEVES CALATRAVA, INGRID
NOLLA ANGUERA, JORDI
ORDÓÑEZ VIVANCO, YADIRA
PASTELLS DÍEZ, CARME
PAU CABELLO, ANA
PAULME, CAMILLE
PEMARTIN, KELLY LIDIA
PETANÁS ESTEBAN, SALVADOR
PUIGMARTI BORRELL, MARC
QUINTANA, MIREIA
RODRÍGUEZ RODRÍGUEZ, CARLOS
ROLDÁN, RAQUEL
ROSA EXPOSITO, MÓNICA
SANCHEZ MARTINEZ, MELCHOR
SANLLEHÍ FIGUEROLA, POL
SEDOUI, ALICIA
SERRA PONT, ANNA
SILVAN, BALTAZAR
SOLER CASAPONSA, ANNA
SZEKRENYI, ANNA
TINTORÈ GASULLA, MARIA
TORT ESCRIBÀ, NURIA
TRAPERO, ANA
VASCONCELOS PACHECO, AIMEE
VAZQUEZ, LAURA
VIDAL MOSQUERA, MIQUEL
VILA ROCA, ESTER
VILANOVA GARCÍA, NEUS
VOGEL, TASSILO

TECHNICIAN

BAENA PÉREZ, BÁRBARA
BLEDA HERNANDEZ, MARIA JOSÉ
GONZALEZ GONZALEZ, ANA
LASTRE, CRISTIAN
LÓPEZ SANTANA, DANIEL
MARTÍNEZ RODRÍGUEZ,, VANESSA
PAUS, ANNA
RAYO PIZARROSO, PEDRO
RIBOSA FORNOVI, ISABEL
ROZALEN MECA, JUANA Mª
RUIZ ARRIBAS, MARTA
ULLDEMOLINS, RAYMOND

POST-GRADUATE, TFG AND UNDERGRADUATE STUDENTS

ALATI, MARCO
BAUTISTA PÉREZ, MARIA ELENA
BERNABÉ MURCIA, ANA ISABEL
GRANADOS, ALBA
GUILLÉN, ANA
JIMENEZ, MARCOS
LO-RE, SARA
MARTINEZ, DEBORA
RICART, MARIA
RODRIGUEZ, ANA
SANCHEZ GARCIA, CARLOS
SANZ DE MADRID, BEATRIZ
SOBREVIAS, LAURA
TURU, MARTA
VIDAL ALTEMIR, BERTA
WOLF, PHILIPP

FOREIGN EXCHANGE STUDENTS

KRISTINA LANG
VALERIA PETTRIZELLI
ALBOQUERS, JANA
BIRENBAUM, CAMILLE
BOURGAREL, CLAIRE
CARRASCO, ESTEFANIA
LOUIS, CHARLENE

List of publications of IQAC ordered by impact factor

2012 (average impact factor $IF_{1/2}$ = 4.184: ——).

Publicació	Nº	IF	Clas.
Angew. Chem. Int. Ed.	1	13.455	ISI
PLoS Biol	1	11.452	ISI
Prog. Lipid Res.	1	10.667	ISI
J. Am. Chem. Soc.	3	9.907	ISI
Energ. Environ. Sci.	1	9.610	ISI
Small	2	8,349	ISI
Nucleic Acids Res.	1	8.026	ISI
Curr. Opin. Colloid Interface Sci.	2	8.010	ISI
Chem. Sci.	1	7.525	ISI
Phys. Rev. Lett.	1	7.370	ISI
Mol. Ther.	1	6.873	ISI
Green Chem.	2	6.320	ISI
J. Invest. Dermatol.	1	6.314	ISI
Chem. Commun.	2	6.169	ISI
Chem.-Eur. J.	4	5.925	ISI
Anal. Chem.	1	5.856	ISI
Biosens. Bioelectron.	2	5.602	ISI
J. Lipid. Res.	1	5.559	ISI
J. Med. Chem.	3	5.248	ISI
Environ. Sci. Technol.	1	5.228	ISI
J. Chem. Theory Comput.	1	5.525	ISI
Biochim. Biophys. Acta - Gen. Subjects	1	5.000	ISI
Bioconjugate Chem.	1	4.930	ISI
Curr. Med. Chem.	1	4.859	ISI
J. Phys. Chem. C	2	4.805	ISI
Mol. Pharmaceut.	1	4.782	ISI
J. Biol. Chem.	1	4.773	ISI
Int. J. Biochem. Cell Biol.	1	4.634	ISI
Inorg. Chem.	1	4.601	ISI
J. Org. Chem.	2	4.450	ISI
Breast Cancer Res. Treat.	2	4.431	ISI
Soft Matter.	3	4.390	ISI
Mol. Nutr. Food Res.	1	4.301	ISI
Langmuir	10	4.186	ISI
J. Hazard. Mater.	2	4.173	ISI
PLoS ONE	2	4.092	ISI
Methods	1	4.011	ISI
Sens. Actuator B-Chem.	1	3.898	ISI
Curr. Pharm. Design	1	3.870	ISI
Electrochim. Acta	1	3.832	ISI
Talanta	2	3.794	ISI
Anal. Bioanal. Chem.	5	3.778	ISI
J. Phys. Chem. B	1	3.696	ISI
Org. Biomol. Chem.	1	3.696	ISI
Food Chem.	2	3.655	ISI
Biophys. J.	2	3.653	ISI
Phys. Chem. Chem. Phys.	1	3.573	ISI
Expert Opin. Ther. Pat.	1	3.571	ISI
Microb. Cell Fact	1	3.552	ISI
Chem. Eng. J.	1	3.461	ISI
Colloid. Surface B	1	3.456	ISI
Polymer	1	3.438	ISI
ACS Med. Chem. Lett.	1	3.355	ISI
Int. J. Pharmaceut.	2	3.350	ISI
Electrophoresis	1	3.303	ISI
Sci. Total Environ.	1	3.286	ISI
J. Mass. Spectrom.	1	3.268	ISI
Amino Acids	2	3.248	ISI
J. Environ. Manage.	1	3.245	ISI
Reprod. Toxicol.	1	3.226	ISI
Mol. Divers	1	3.153	ISI
ChemMedChem	1	3.151	ISI
Food Res. Int.	1	3.150	ISI
J. Nat. Prod.	1	3.128	ISI
J. Colloid. Interf. Sci.	2	3.070	ISI
Curr. Org. Chem.	1	3.064	ISI
J. Pharm. Sci.	1	3.055	ISI
J. Biotechnol.	1	3.045	ISI
Brt. J.Nutr.	2	3.013	ISI
Food Chem. Toxicol.	1	2.999	ISI
J. Phys. Chem. A	1	2.946	ISI
Bioorgan. Med. Chem.	2	2.921	ISI
Electroanal.	1	2.872	ISI
J. Agr.Food Chem.	5	2.823	ISI
J. Photoch. Photobio. B	2	2.814	ISI
Eur. Polym. J.	1	2.739	ISI
J. Mol. Catal. B: Enzym.	1	2.735	ISI
Tetrahedron Letters	1	2.683	ISI
J. Chem. Ecol.	1	2.657	ISI
J. Biomed. Mater. Res. A	1	2.625	ISI
New J. Chem.	1	2.605	ISI
Chem. Phys. Lipids.	1	2.571	ISI
Bioorg. Med. Chem. Lett.	1	2.554	ISI
Synthesis	1	2.466	ISI
Molecules	3	2.386	ISI
Int. J. Life Cycle Ass.	1	2.362	ISI
Colloid Polym. Sci	1	2.331	ISI
Phys. Rev. E	1	2.255	ISI
Colloid Surf. A: Physicochem. Eng. Asp.	1	2.236	ISI
Eur. Biophys. J. Biophys. Lett.	1	2.139	ISI
Biodegradation	1	2.017	ISI
Clin. Rheumatol.	1	1.996	ISI
Chem. Biodivers.	1	1.804	ISI
J. Pept. Sci.	1	1.799	ISI
Luminescence	2	1.731	ISI
J. Pharm. Pharm. Sci.	1	1.646	ISI
Polym. Eng. Sci.	1	1.302	ISI
Text. Res. J.	1	1.122	ISI
Biocatal. Biotransfor.	1	0.905	ISI
J. Text. I.	1	0.514	ISI
J. Soc. Leath. Techn. and Chem.	1	0.436	ISI
Chemistry Open	1	----------	Non-ISI
International Dyer	1	----------	Non-ISI
J. Chem. Biol.	1	----------	Non-ISI
NCP-Noticias de Cosmética y Perfumería	1	----------	Non-ISI
RSC Adv.	1	----------	Non-ISI
JIMD Rep.	1	----------	Non-ISI
Acta Horticulturae	1	----------	Book
Advances in Organic Synthesis	1	----------	Book
Green Processes. V8: Green Nanoscience	1	----------	Book
Methods in Molecular Biology	3	----------	Book
Smart Nanoparticles Technology	1	----------	Book
Supram. Chem.: From Molec. to Nanomat.	1	----------	Book
Topics in the Colloidal Aggregation and...	1	----------	Book

2013 (average impact factor $IF_{½}$= 4,064: ——).

Journal	Nº	IF	Class.
Nature	1	38.597	ISI
Angew Chem Int Edit	2	13.734	ISI
Nano Lett	1	13.025	ISI
Acs Nano	1	12.062	ISI
J Am Chem Soc	1	10.677	ISI
Cell Death And Differentiation	1	8.371	ISI
Chem Sci	1	8.314	ISI
Embo Mol Med	1	7.795	ISI
J Controlled Release	1	7.633	ISI
Biomaterials	1	7.604	ISI
Oncogene	1	7.357	ISI
Mol Ther	1	7.041	ISI
Green Chem.	1	6.828	ISI
Oncotarget	1	6.636	ISI
Chem Commun	3	6.378	ISI
Adv Cancer Res	1	6.351	ISI
Ann Surg	1	6.329	ISI
J Mater Chem. B	2	6.101	ISI
Chem-Eur J	2	5.831	ISI
Faseb J	1	5.704	ISI
Carcinogenesis	1	5.635	ISI
J Med Chem	2	5.614	ISI
Int J Cardiology	1	5.509	ISI
Biosens Bioelectron	2	5.437	ISI
Free Radical Bio Med	1	5.271	ISI
J Biomedical Nanotechnology	1	5.256	ISI
Acs Appl Mater Inter	1	5.008	ISI
Water Res	1	4.655	ISI
J Org Chem	1	4.564	ISI
Electrochem Commun	1	4.425	ISI
J Lipid Res	1	4.386	ISI
Pharmacological Research	1	4.346	ISI
Toxicol. Sci.	1	4.328	ISI
Arthritis Research & Therapy	1	4.302	ISI
Database	1	4.200	ISI
Langmuir	6	4.187	ISI
Tissue Eng	1	4.065	ISI
Nutr Metab Cardiovas	1	3.978	ISI
J Hazardous Materials	2	3.925	ISI
Obesity	1	3.922	ISI
Soft Matter	2	3.909	ISI
Bba-Gen Subjects	1	3.848	ISI
Phys Chem Chem Phys	4	3.829	ISI
Eur J Pharm Biopharm	2	3.826	ISI
Faraday Discuss.	2	3.821	ISI
Chembiochem	3	3.740	ISI
Plasma Process Polym	1	3.730	ISI
Plos One	3	3.730	ISI
Curr Top Med Chem	2	3.702	ISI
Anal Bioanal Chem	3	3.659	ISI
Stem Cell Res Ther	1	3.652	ISI
J Phys. Chem. B	2	3.607	ISI
Org Biomol Chem	2	3.568	ISI
Colloid Surface B	2	3.554	ISI
Sensor Actuat B-Chem	1	3.535	ISI
Eur J Med Chem	1	3.499	ISI
Chem Eng J	1	3.473	ISI
Int J Pharmaceut	1	3.458	ISI
Micropor Mesopor Mat	1	3.365	ISI
Chemphyschem	1	3.349	ISI
Food Chem	1	3.334	ISI
Future Med Chem	1	3.310	ISI
J Biotechnology	1	3.183	ISI
J Colloid Interf Sci	3	3.172	ISI
Exp Eye Res	1	3.026	ISI
Food Res Int	1	3.005	ISI
New J Chem	1	2.966	ISI
J Agr Food Chem	2	2.906	ISI
J Biomed Mater Res A	1	2.834	ISI
J Mol Catal B-Enzym	1	2.823	ISI
Steroids	1	2.803	ISI
J Phys. Chem. A	1	2.771	ISI
Mol Biochem Parasit	1	2.734	ISI
Prostag Leukotr Ess	1	2.732	ISI
Med. Chem. Commun.	1	2.722	ISI
Pest Manag Sci	2	2.594	ISI
Enzyme Microb Tech	1	2.592	ISI
Rsc Adv	3	2.562	ISI
Int J Mol Sci	1	2.464	ISI
J Chem Ecol	1	2.462	ISI
Bioorg Med Chem Lett	1	2.338	ISI
Eur Biophys J Biophy	1	2.274	ISI
Materials	2	2.247	ISI
Catal Lett	1	2.244	ISI
Colloid Polym Sci	2	2.161	ISI
Tetrahedron-Asymmetr	1	2.115	ISI
Pestic Biochem Phys	1	2.111	ISI
Colloid Surface A	1	2.108	ISI
Lipids In Health and Disease	1	2.015	ISI
Thermochim Acta	1	1.989	ISI
J Surfactants Deterg	1	1.515	ISI
J Appl Polym Sci	2	1.395	ISI
Mycoses	1	1.278	ISI
Polymer Engineering & Science	1	1.243	ISI
J Nanosci Nanotechno	1	1.149	ISI
Text Res J	2	1.135	ISI
Fibers And Polymers	1	0.912	ISI
J Insect Sci	1	0.875	ISI
J Macromol Sci A	2	0.807	ISI
J Soc Leath Tech Ch	1	0.648	ISI
J Am Leather Chem As	2	0.644	ISI
J Of Chemistry	1	0.484	ISI
Aitex Review	1	----------	Non-ISI
Colloid And Interface Chem For Nanotech	1	----------	Book
Comprehensive Analytical Chemistry	1	----------	Book
Emulsion Formation And Stability	2	----------	Book
Guanine Quartets-Structure and Applic.	2	----------	Book
Int J Environ Waste Manag	1	---------	Non-ISI
Int J Cosmetic Science	1	----------	Non-ISI
Intrinsically Disordered Proteins	1	----------	Non-ISI
Isrn Biochemistry	1	----------	Non-ISI
J Drug Delivery	1	----------	Non-ISI
Modern Methods in Stereosel. Aldol React.	1	----------	Book
Peptide Synth Applic. Methods Mol Biol	1	----------	Book
Textile Asia	1	----------	Non-ISI
The Handbook Of Environmental Chemistry	5	----------	Book