



The Carbohydrate Chemistry Group



**Principal
Investigator**



**Prof. Dr.
Amélia Pilar Rauter**

CCG-CQB | FCUL

<http://cqb.fc.ul.pt/research/carbohydrate-chemistry/>



The Carbohydrate Chemistry Group

Center of Excellence of Euroglycosciences Forum

(approved for 2009-2014 by the ESF)

Presently
15 Members

PI + 1 Senior Researcher
1 FCT Investigator
1 Post Doc
7 PhD Students (2 PhD studentships in industry)
2 Research Fellows
2 MSc Students

Projects

Funded by EU: **2** (2013-2016 and 2014-2018)
Funded by PCBNet: **2** (2011-2012 and 2012-2013)
Funded by QREN: **1** (2011-2014)
Funded by FCT: **3** (2013-2015 and 2008-2011)



ca. 1.5
millions euro



The Carbohydrate Chemistry Group

**Sugars and/or
natural
resources**

*Based on a
sustainable model*

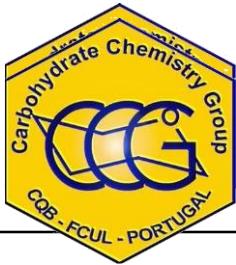
Drug candidates

Functional food ingredients for
pharmaceutical / food industries

Economic and social
benefits in terms
of **prevention of
functional decline and
ageing, nutrition, health
and biosecurity.**

Strategic areas:

- New approaches towards healthy ageing included in the activities of the
- **EIP- AHA Action Plan 3** on prevention of functional decline.
- **Sustainable Chemistry** for Functional Molecules.
- **Functional food ingredients, therapeutics and mechanisms of action.**



The Carbohydrate Chemistry Group

Research based on:

Generation of new molecular entities

- Design and synthesis
- Environmentally friendly methodologies
- Isolation from natural resources and structure elucidation

Polyphenols chemistry and society

- Functional foods
- Biomass residues valorisation
- Cultural heritage

Challenges

- New leads for degenerative (**cancer**) and amyloid diseases (**Alzheimer's disease, diabetes**)
- Sugar-based bactericides towards **biosecurity**
- Functional foods for a healthy ageing



The Carbohydrate Chemistry Group

Papers in

1% more cited journals

10% more cited

2008-2012

8% of papers

44% of papers

2013-2014

11% of total of papers

47% of papers

Journal of
**Medicinal
Chemistry**

Article
pubs.acs.org/jmc

Exploiting the Therapeutic Potential of
8- β -D-Glucopyranosylgenistein: Synthesis, Antidiabetic Activity, and
Molecular Interaction with Islet Amyloid Polypeptide and Amyloid
 β -Peptide (1–42)

Ana R. Jesus,[†] Catarina Dias,[†] Ana M. Matos,^{†,‡,§} Rodrigo F. M. de Almeida,[†] Ana S. Viana,[†]
Filipa Marcelo,^{||} Rogério T. Ribeiro,^{‡,§} Maria P. Macedo,^{‡,§} Cristina Airoldi,[†] Francesco Nicotra,[†]
Alice Martins,[†] Eurico J. Cabrita,^{||} Jesús Jiménez-Barbero,[#] and Amélia P. Rauter*,[†]

**2nd most cited journal in
the field of
multidisciplinary
chemistry**

**Angewandte
International Edition
Chemie**

Glycosides

DOI: 10.1002/anie.201405008

**gem-Difluorocarbadisaccharides: Restoring the *exo*-Anomeric
Effect****

Bixue Xu, Luca Unione, Joao Sardinha, Shaoping Wu, Mélanie Ethève-Quelquejeu,
Amelia Pilar Rauter, Yves Blériot, Yongmin Zhang, Sonsoles Martín-Santamaría, Dolores Díaz,
Jesus Jiménez-Barbero,* and Matthieu Sollogoub*

**1st most cited
journal in the field of
medicinal chemistry**



CCG Networking



EUROPEAN INNOVATION PARTNERSHIP

on Active and Healthy Ageing

EIP AHA

INOVAFUNAGEING commitment

Healthy Ageing with innovative functional foods/leads for
degenerative and metabolic diseases

Action group 3: Prevention and early diagnosis of frailty and
functional decline, both physical and cognitive, in older people



CCG Networking



EIP-AHA A3 Activities



Intersectoral knowledge transfer and research training
Advances in several areas of basic research, in diagnostics and therapeutics development

“Diagnostic and Drug Discovery Initiative for Alzheimer’s Disease”

Industry-Academia Partnerships and Pathways (IAPP), FP7-PEOPLE-2013-IAPP,
Project Nr. 612347, 2014-2018.

- **Coordination:** University of Sheffield (UK)
- **Participant institutions:** FCUL, Eli Lilly and Company (UK), Amorfix Life Sciences Ltd (Canada) and Biofordrug (Italy)
- **PI FCUL:** A. P. Rauter

Enhance EU standing and international competitiveness in this extremely challenging technological areas.



CCG Networking



EIP-AHA A3 Activities



"PERsonalised ICT supported Service for Independent Living and Active Ageing"

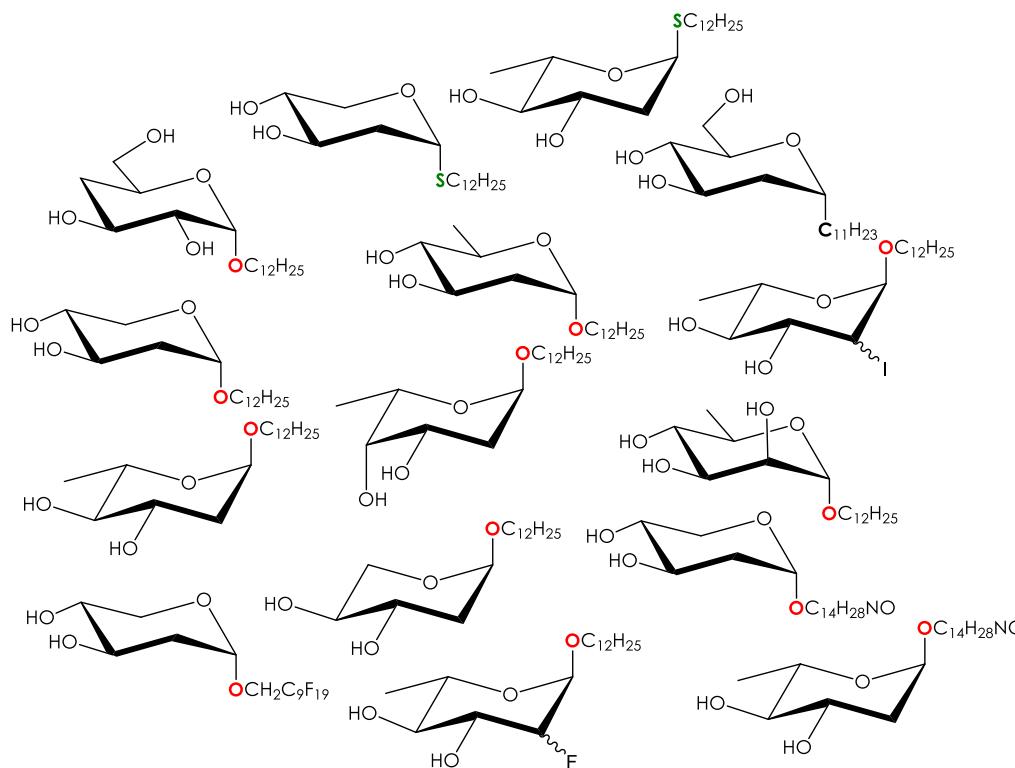
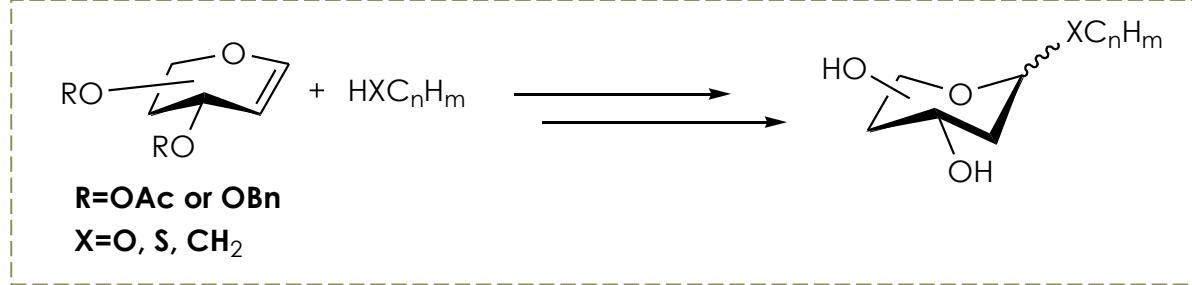
Research project STREP, FP7-ICT-2013-10, Project Nr. 610359, 2013-2016.

- **Coordination:** Universiteit Twente (Netherlands)
- **Participant Institutions:** FFCUL and FCUL (third party), among other institutions from The Netherlands, Italy, Ireland, Spain, and the company Nexera (Italy)
- **PI FFCUL-FCUL** and workpackage 3 leader: A. P. Rauter.

FACIB | New drugs from sugars against *Bacillus* infection

Exploiting alkyl deoxy glycosides as antimicrobial agents

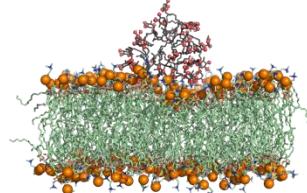
Synthesis



FACIB | New drugs from sugars against *Bacillus* infection

Exploiting alkyl deoxy glycosides as antimicrobial agents

Interaction with cell membranes

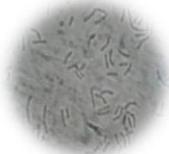


ITCG CQB

Biological activity against *Bacillus anthracis*



INSA

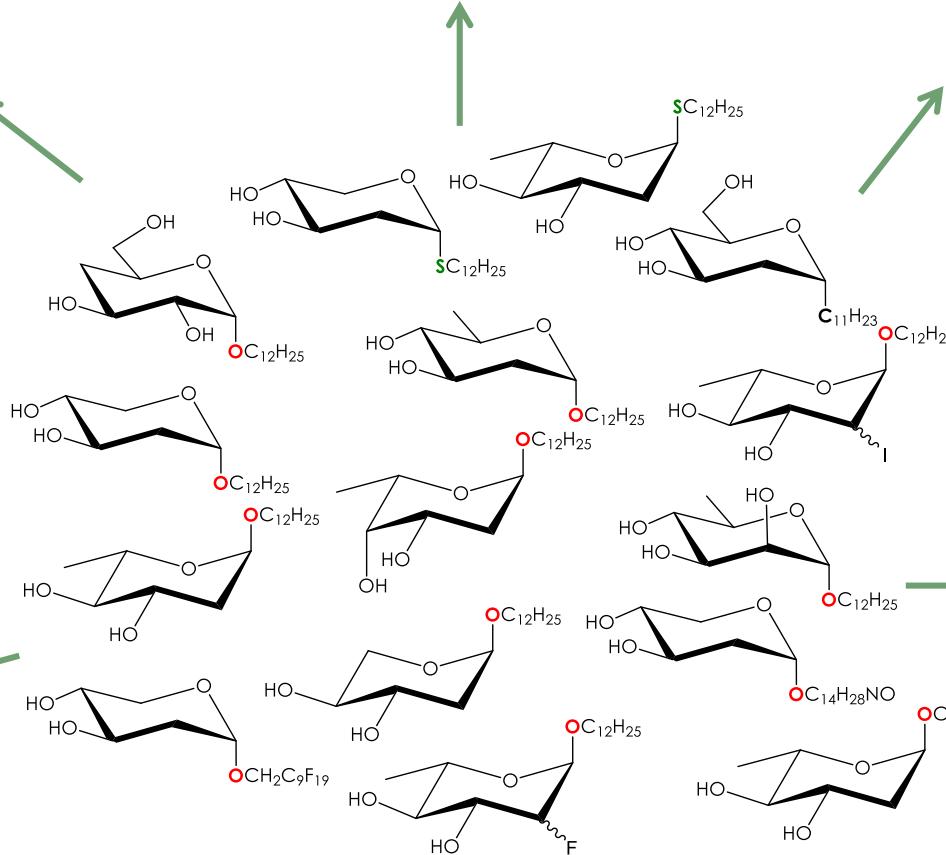
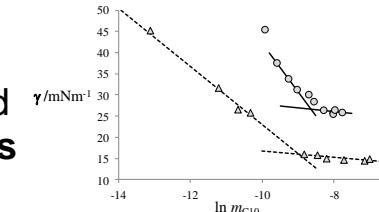


Biological activity against *Bacillus cereus*.

BioFIG
Center for Biodiversity, Functional and Integrative Genomics

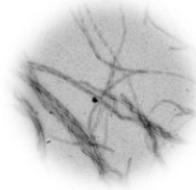
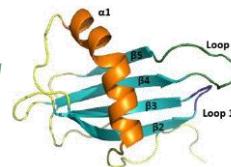
SRG CQB

Surface activity and adsorption properties



The University Of Sheffield.

Infection and Ageing
Interaction with amyloid peptides



Cipan

Scale-up
Academia-Industry collaboration

QR
EN
QUADRO DE REFERÊNCIA ESTRATÉGICO NACIONAL PORTUGAL 2007-2013

FACIB | New drugs from sugars against *Bacillus* infection

Exploiting alkyl deoxy glycosides as antimicrobial agents

FACIB project (QREN SI I&DT co-promotion program, Lisboa 01-0202-FEDER-021547); 2011-2014



Dr. Alice Martins
Post Doc
Catarina Dias
PhD
Studentship in
Industry



João P. Pais
PhD
Studentship in
Industry



**Vasco
Cachatra**
PhD student



Rafael Nunes
MSc student



Patrícia Serra
Research fellow



Filipa Almeida
Research fellow

Publications

A. Martins, M. S. Santos, C. Dias, P. Serra, V. Cachatra, J. Pais, J. Caio, V. H. Teixeira, M. Machuqueiro, M. S. Silva, A. Pelerito, J. Justino, M. Goulart, F. V. Silva, A. P. Rauter. *Eur. J. Org. Chem.* **2013**, 8, 1448.

F. V. M. Silva, M. Goulart, J. Justino, A. Neves, F. Santos, J. Caio, S. Lucas, A. Newton, D. Sacoto, E. Barbosa, M. S. Santos, A.P. Rauter, *Bioorg. Med. Chem.* **2008**, 16(7), 4083.

A.P. Rauter, T. Almeida, A. I. Vicente, V. Ribeiro, J. C. Bordado, J. P. Marques, F. Ramôa-Ribeiro, M. J. Ferreira, C. Oliveira, M. Guisnet. *Eur. J. Org. Chem.* **2006**, 2006(10), 2429.

A.P. Rauter, S. Lucas, T. Almeida, D. Sacoto, V. Ribeiro, J. Justino, A. Neves, F. V. M. Silva, M. C. Oliveira, M. J. Ferreira, M.-S. Santos, E. Barbosa. *Carbohydr. Res.* **2005**, 340(2), 191.

Book Chapters

C. Dias, A. Martins, M. S. Santos, A. P. Rauter, M. Malik; In: **Carbohydrate Chemistry - Proven Synthetic Methods** (Ed. S. Vidal), Vol. 3, CRC Press - Taylor & Francis: Boca Raton, Florida, 2014, in press.

C. Dias, A. P. Rauter, In: **Carbohydrates in Drug Design**, Ed. J. Jiménez Barbero, The Royal Society of Chemistry, Cambridge, 2014, in press

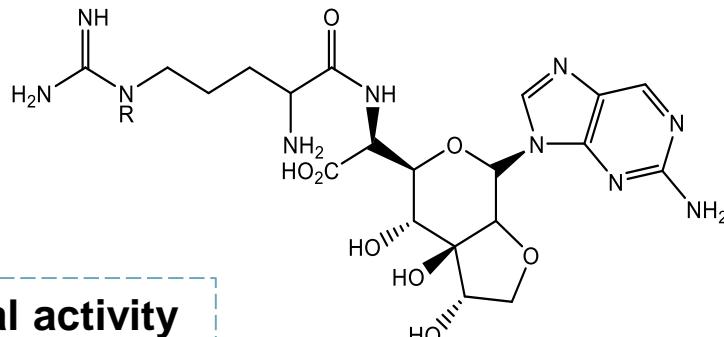
Patent

A. P. Rauter, A. Martins, J. Caio, J. P. Pais, P. Serra, M.-S. Santos, A. Pelerito, J. P. Gomes, J. Justino, R. Dias, R. Tenreiro WO 2012095792 A1 (submission: 10-01-2012, pub. date: 19-07-2012).



Anticholinergic Nucleosides | Studies on the sugar core

Antitumor activity and selective BChE inhibition

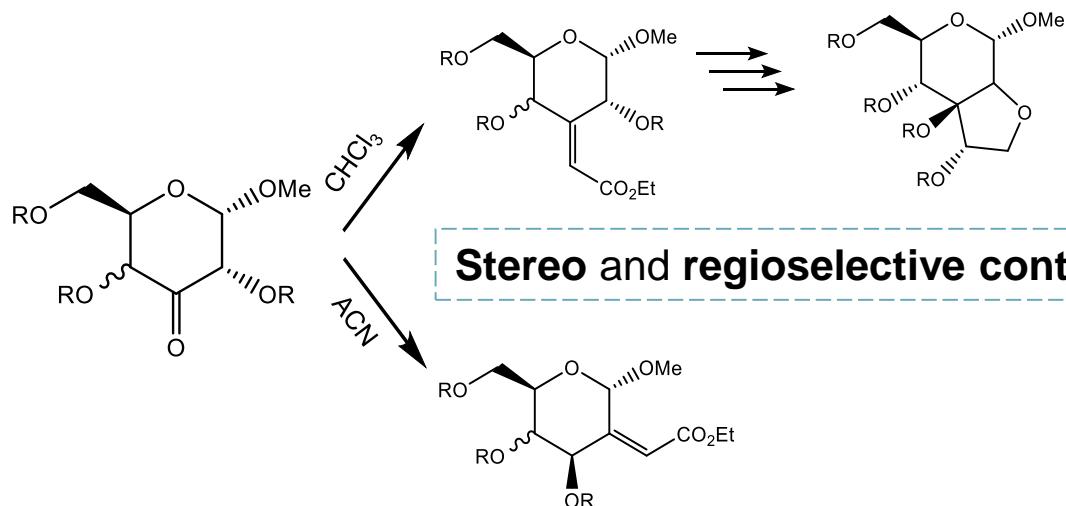


Antifungal activity



Filipa Marcelo
Previous member

Marcelo, F.; Jiménez-Barbero, J.; Marrot, J.; Rauter, A. P.; Sinaÿ, P.; Blériot, Y. Stereochemical Assignment and First Synthesis of the Core of Miharamycin Antibiotics. *Chem. Eur. J.* **2008**, 14, 10066



Stereo and regioselective control



Vasco Cachatra
PhD student

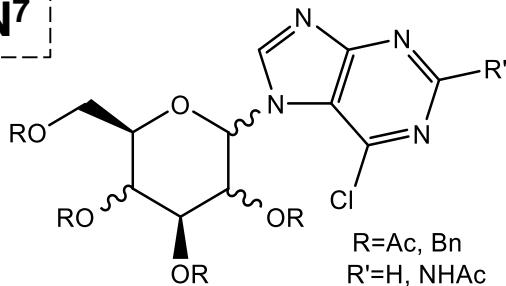


Filipa Almeida
Research Fellow

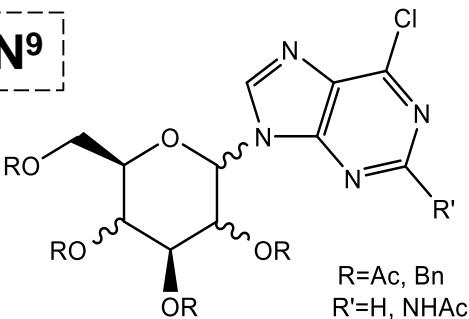
Anticholinergic Nucleosides

Antitumor activity and selective BChE inhibition

N⁷



N⁹



Structural requirements:

- N⁷ linked ACP
- Mannosyl moiety
- α configuration



Nuno Xavier
FCT Investigator



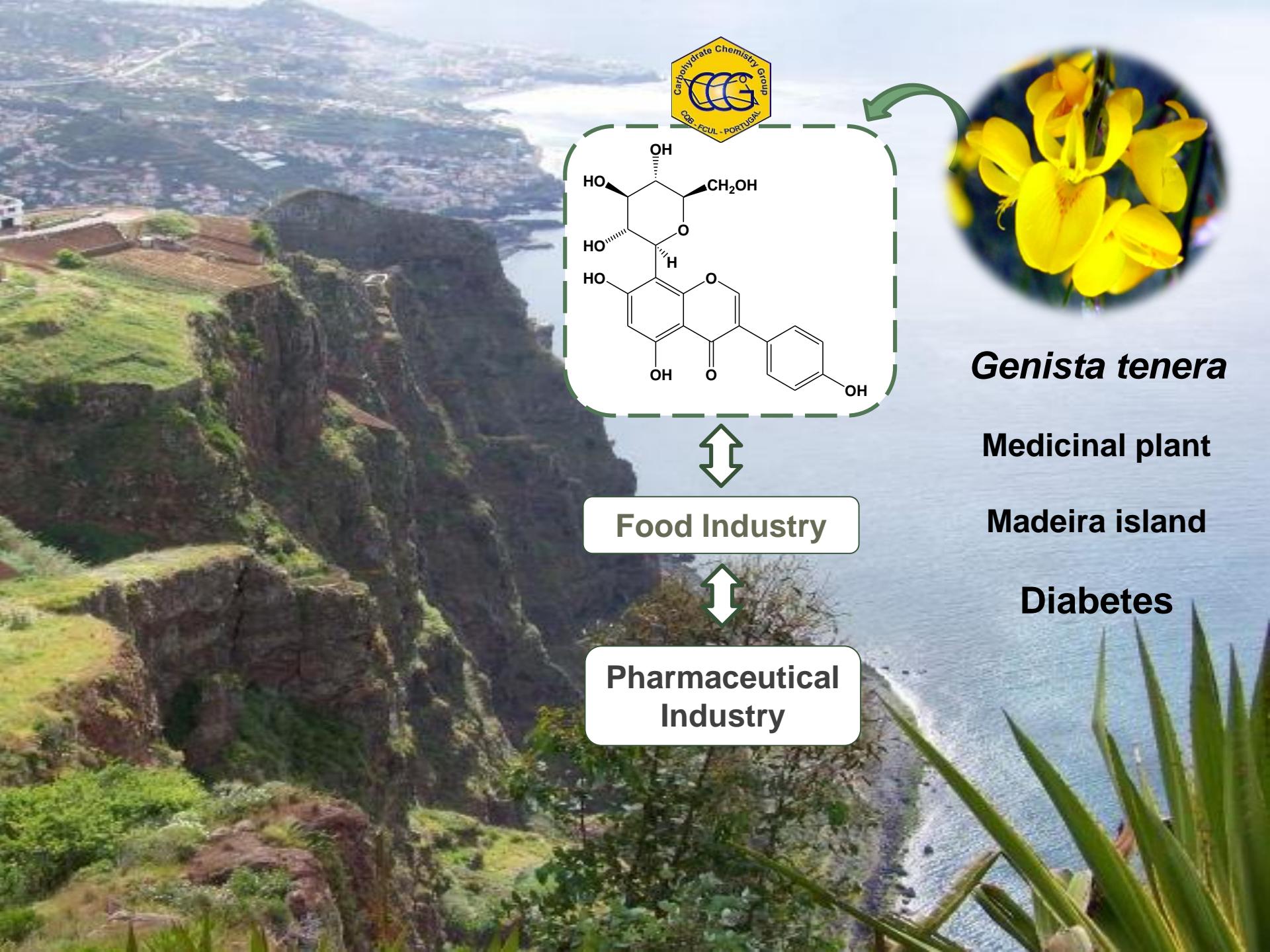
Sven Bettermann
Visiting MSc Student



Stefan Schwarz
Previous Member

Publications:

- Marcelo, F.; Silva, F. M. S.; Goulart, M.; Justino, J.; Sinaÿ, P.; Blériot, Y; Rauter, A. P. *Bioorg. & Med. Chem.* **2009**, *17*, 5106
- Schwarz, S.; Csuk, R.; Rauter, A. P. *Org. Biomol. Chem.* **2014**, *12*, 2446
- Xavier, N. M.; Schwarz, S.; Vaz, P. D.; Czuk, R.; Rauter, A. P. *Eur. J. Org. Chem.* **2014**, *2014*, 2779



Genista tenera

Medicinal plant

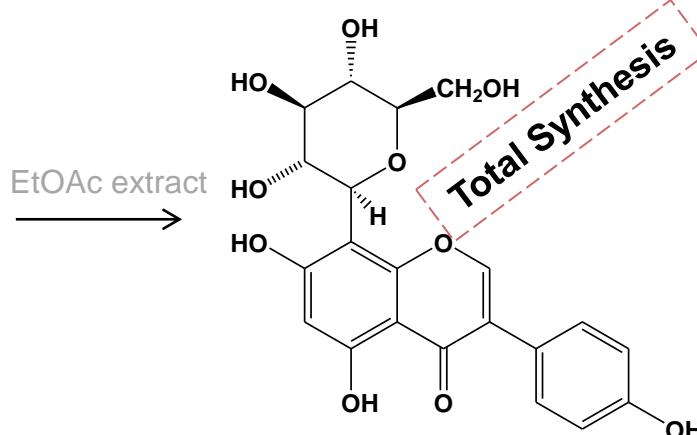
Madeira island

Diabetes

Food Industry

Pharmaceutical
Industry

***Genista tenera* | A natural source of antidiabetic compounds with new mechanisms of action**



8-B-D-GLUCOSYLGENTIESTIN

- Normalizes fasting and postprandial hyperglycemia
- Better α-glucosidase inhibitor than acarbose
- Nontoxic
- Suppresses hIAPP fibril formation
- Interacts with hIAPP and amyloid β oligomers

Exploiting the Therapeutic Potential of 8-β-D-Glucopyranosylgenistein: Synthesis, Antidiabetic Activity, and Molecular Interaction with Islet Amyloid Polypeptide and Amyloid β-Peptide (1–42)

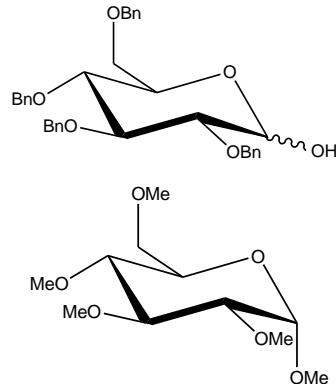
Ana R. Jesus,[†] Catarina Dias,[†] Ana M. Matos,^{†,‡} Rodrigo F. M. de Almeida,[†] Ana S. Viana,[†] Filipa Marcelo,^{||} Rogério T. Ribeiro,^{‡,§} Maria P. Macedo,^{‡,§} Cristina Airoldi,[⊥] Francesco Nicotra,[⊥] Alice Martins,[†] Eurico J. Cabrita,^{||} Jesús Jiménez-Barbero,[#] and Amélia P. Rauter*,[†] October 2014

A.P. Rauter, A. Jesus, A. Martins, C. Dias, Rogério Ribeiro, M.- P. Macedo, J. Justino, H. Mota-Filipe, R. Pinto, B. Sepedes, M. Medeiros, J. Barbero, C. Airoldi, F. Nicotra WO 2013132470 A2 September 2013

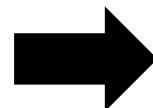
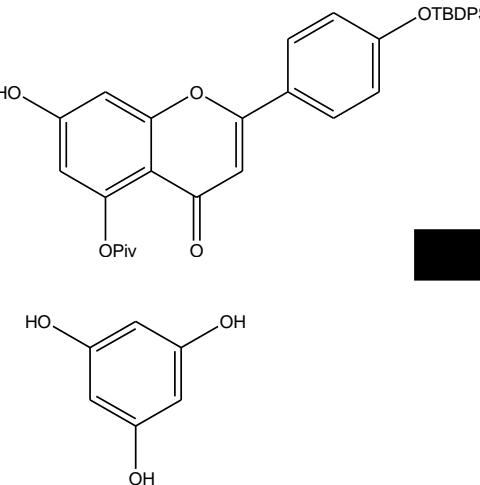


***Genista tenera* | A natural source of antidiabetic compounds with new mechanisms of action**

Glycosyl donors



Glycosyl acceptors



New, more efficient
synthetic approaches



Dr. Alice Martins
Post Doc



Ana Rita Jesus
PhD student



Catarina Dias
PhD Student



**Ana Marta de
Matos**
PhD student

Collaborations:



CEDOC
Chronic Diseases FCM NOVA

FCT
FACULDADE DE
CIÉNCIAS E TECNOLOGIA
UNIVERSIDADE NOVA DE LISBOA

DEGLI STUDI
UNIVERSITÀ
BICOCCA

***Genista tenera* | A natural source of antidiabetic compounds with new mechanisms of action**



**Ana Marta de
Matos**
PhD student

Collaborations:



Future Perspectives 2014-2018

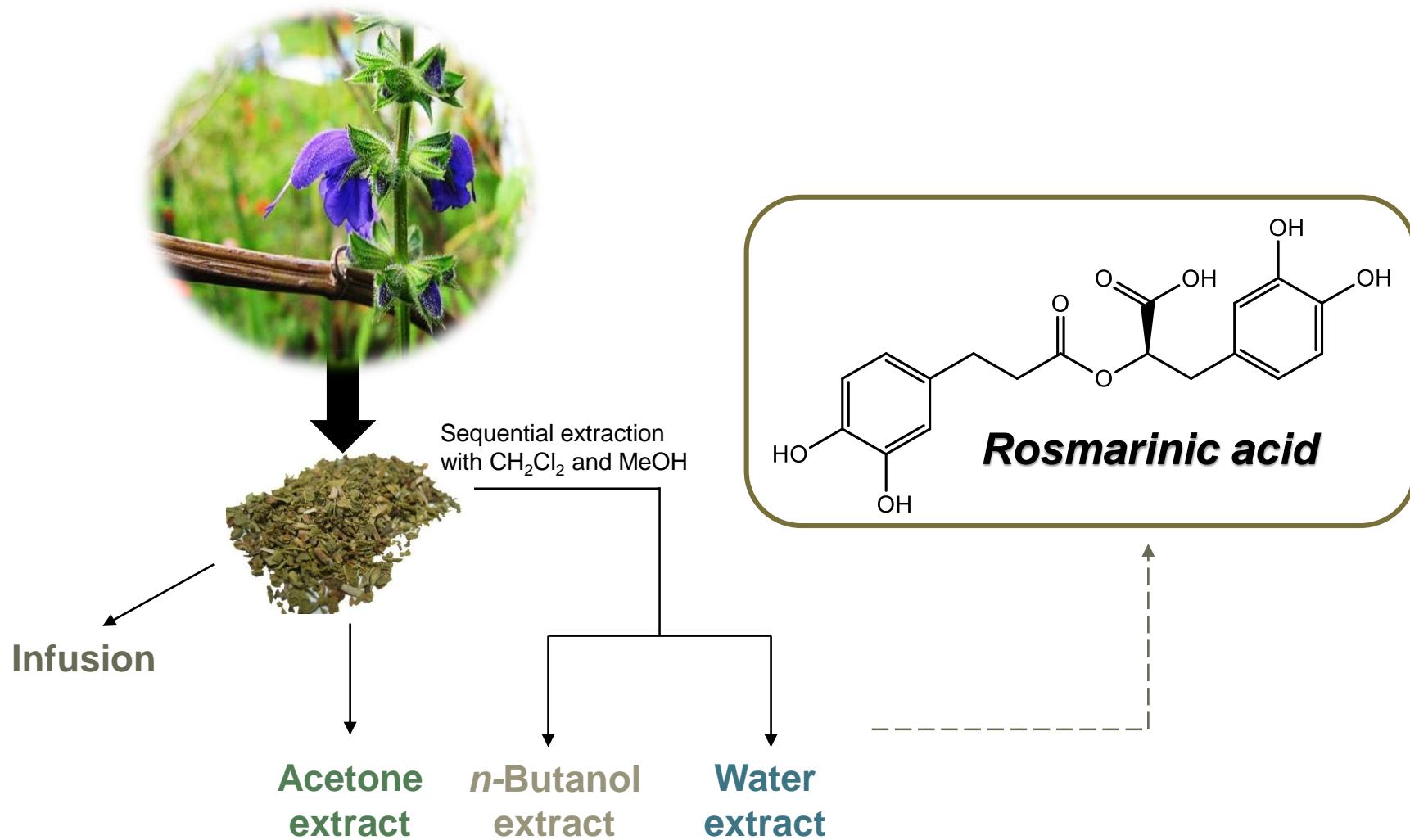
Synthesis:

- Exploratory investigation towards **new synthetic routes** for the lead compound, **8- β -D-glucosylgenistein**
- Development of a **small library of simpler analogue molecules**

Biological assays:

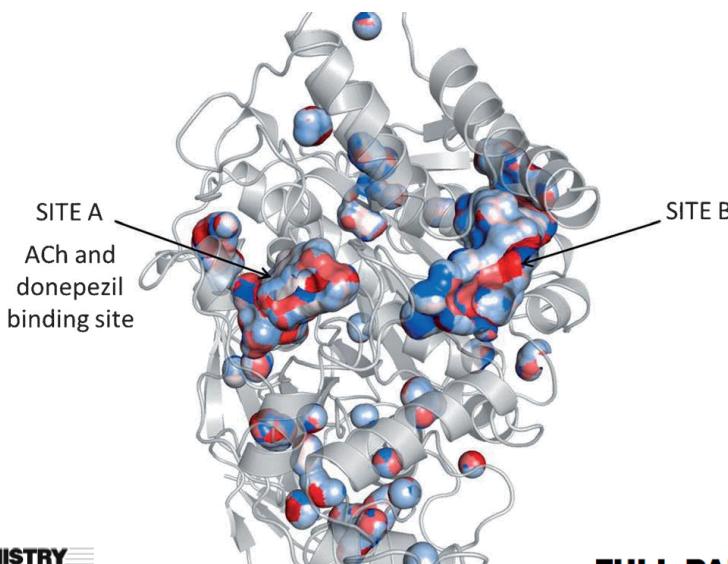
- Disclosure of **mechanisms of action** against T1 and T2 diabetes:
 - Hepatic glucose and lipid metabolism studies
 - Investigation of β -cell regenerating effects
 - Pancreatic histological changes, inflammatory markers and apoptosis in the presence of 8G and analogues
 - RNA sequencing of insulinoma cells treated with 8G and analogues
 - NMR binding experiments
 - Amyloid aggregation studies and research on neuroprotective effects
 - Inhibition of α -glucosidase and glucose-6-phosphatase
 - Determination of **BBB permeability**

***Salvia sclareoides* | New functional food ingredients for neurodegenerative diseases**



***Salvia sclareoides* | New functional food ingredients for neurodegenerative diseases**

Rosmarinic acid is the main compound in the extract interacting with AChE. It does not compete for the same binding site with the traditional AChE inhibitors.



CHEMISTRY
A EUROPEAN JOURNAL

FULL PAPER

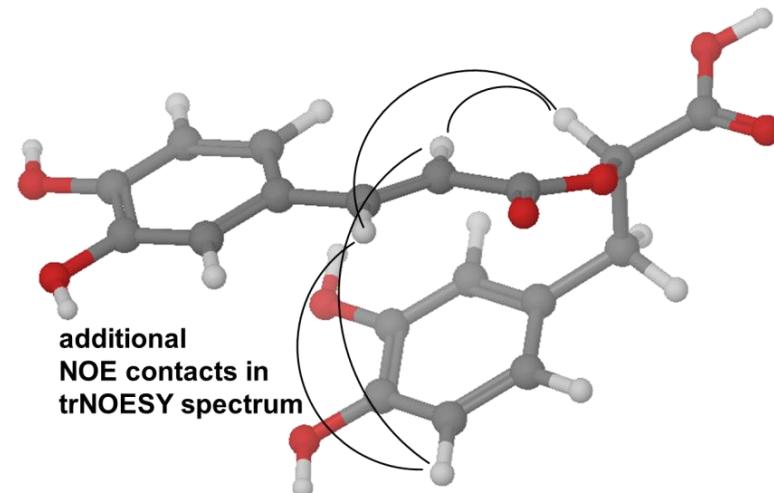
DOI: 10.1002/chem.201203966

Molecular Recognition of Rosmarinic Acid from *Salvia sclareoides* Extracts by Acetylcholinesterase: A New Binding Site Detected by NMR Spectroscopy

Filipa Marcelo,^[a, b, c] Catarina Dias,^[a] Alice Martins,^[a] Paulo J. Madeira,^[a] Tiago Jorge,^[a] M. Helena Florêncio,^[a] F. Javier Cañada,^[b] Eurico J. Cabrita,^[c] Jesús Jiménez-Barbero,^{*[b]} and Amélia P. Rauter^{*[a]}

Marcelo et al., *Chem. Eur. J.* 2013, 19, 6641

Rosmarinic acid interacts with $\text{A}\beta_{1-42}$. Aromatic protons are mostly involved in the binding.



CHEMISTRY
AN ASIAN JOURNAL

DOI: 10.1002/asia.201201063

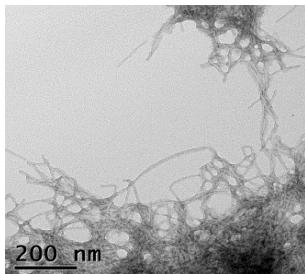
Natural Compounds against Alzheimer's Disease: Molecular Recognition of $\text{A}\beta 1-42$ Peptide by *Salvia sclareoides* Extract and its Major Component, Rosmarinic Acid, as Investigated by NMR

Cristina Aioldi,^{*[a]} Erika Sironi,^[a] Catarina Dias,^[b] Filipa Marcelo,^[b, c] Alice Martins,^[b] Amélia Pilar Rauter,^[b] Francesco Nicotra,^[a] and Jesus Jimenez-Barbero^{*[a, c]}

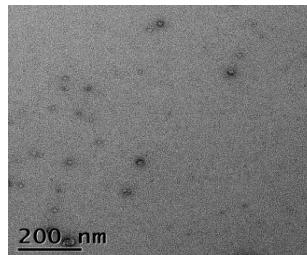
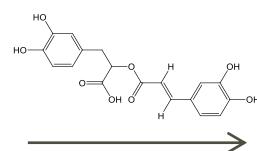
Aioldi et al., *Chem. Asian J.* 2013, 8, 596

***Salvia sclareoides* | New functional food ingredients for neurodegenerative diseases**

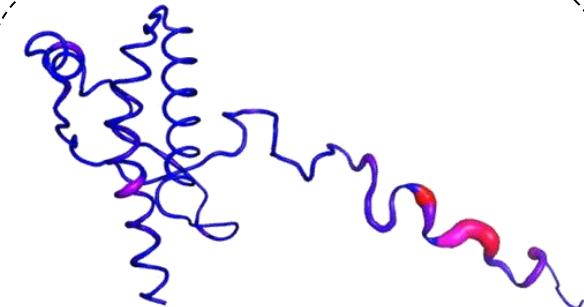
Rosmarinic acid interacts with $\text{A}\beta_{1-42}$ and remove pre-formed cystatin B fibrils to form amorphous aggregate.



Cystatin B



**Cystatin B +
Rsm. acid**



Extracts interact with PrP^{C} and protect cells against PrP^{Sc}

Rosmarinic acid showed resistance against enzymatic digestion



Dr. Alice Martins
Post Doc



Daniela Batista
MSc Student



Catarina Dias
PhD Student



Filipa Marcelo
Previous member

Collaborations:



**The
University
Of
Sheffield.**

Additional publications on the valorization of natural resources | Developing Countries and Emerging Countries: Tunisia, Algeria, Brazil



Publications:



**Maria Eduarda
Araújo**

Senior researcher

Ayda Khadri, Mohamed Neffati, Samira Smiti, Pedro Falé, A. Rosa L. Lino, M. Luisa. M. Serralheiro, M. Eduarda M. Araújo, *LWT - Food Science and Technology*, **2010**, 43, 331

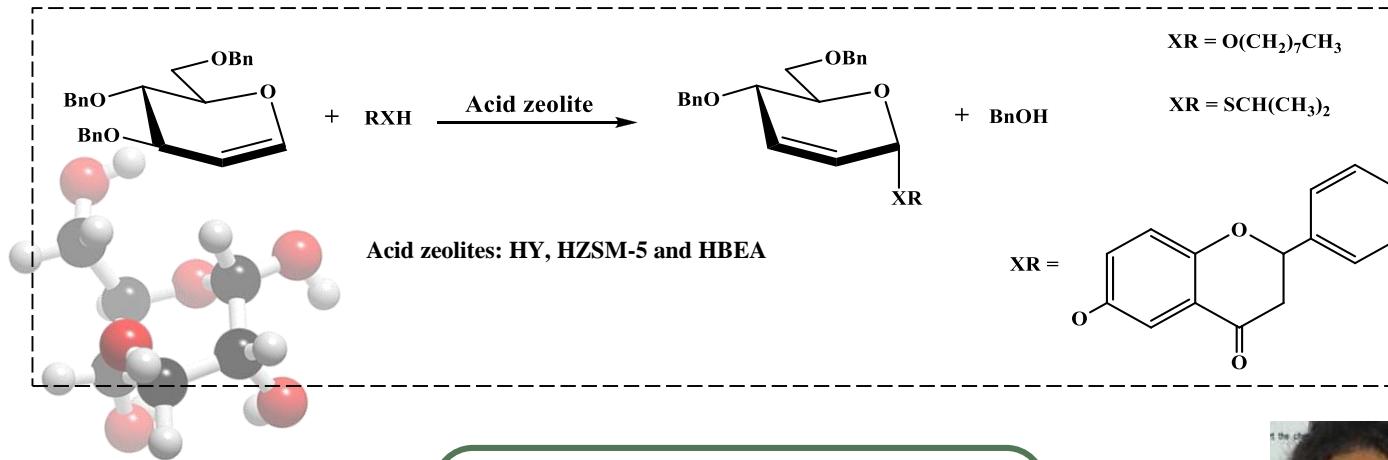
Ayda Khadri, Mohamed Neffati, Samira Smiti, J.M.F. Nogueira, M.E.M. Araújo, *Natural Product Research*, **2011**, 25 (11), 108

Ayda Khadhri, Ridha El Mokni, Carlos Almeida, J.M.F. Nogueira, M. Eduarda M. Araújo, *Industrial Crops and Products*, **2014**, 52, 29

Nadia Amessis-Ouchemoukh, Khodir Madani, Pedro L.V. Falé, M. Luisa Serralheiro, Maria Eduarda M. Araújo, *Industrial Crops and Products*, **2014**, 53, 6

Ayda Khadhri, Intidhar Bouali, Samia Belkhir, Ridha El Mokni, Samira Smiti, Carlos Almeida, J.M.F. Nogueira, M. Eduarda M. Araújo, *Journal of Essential Oil Bearing Plants*, **2014**, 17, 445

Zeolites | New environmentally friendly catalysts for phenols glycosylation



Nuno Xavier
FCT Investigator

O/C-phenol glycosylation
HY zeolite
Montmorillonite K10

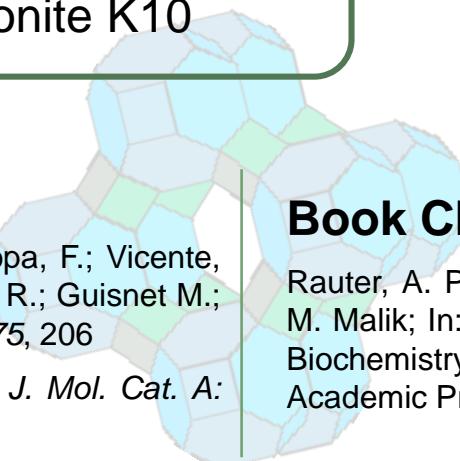


Daniela Batista **Ana Rita Jesus**
MSc Student PhD student

Publications:

Rauter, A. P.; Almeida, T.; Xavier, N. M.; Siopa, F.; Vicente, A. I.; Lucas, S. D.; Marques, J. P.; Ribeiro, F. R.; Guisnet M.; Ferreira, M. J. *J. Mol. Cat. A: Chem.* **2007**, 275, 206

Xavier, N. M.; Lucas, S. D.; Rauter, A. P. . *J. Mol. Cat. A: Chem.* **2009**, 305, 84



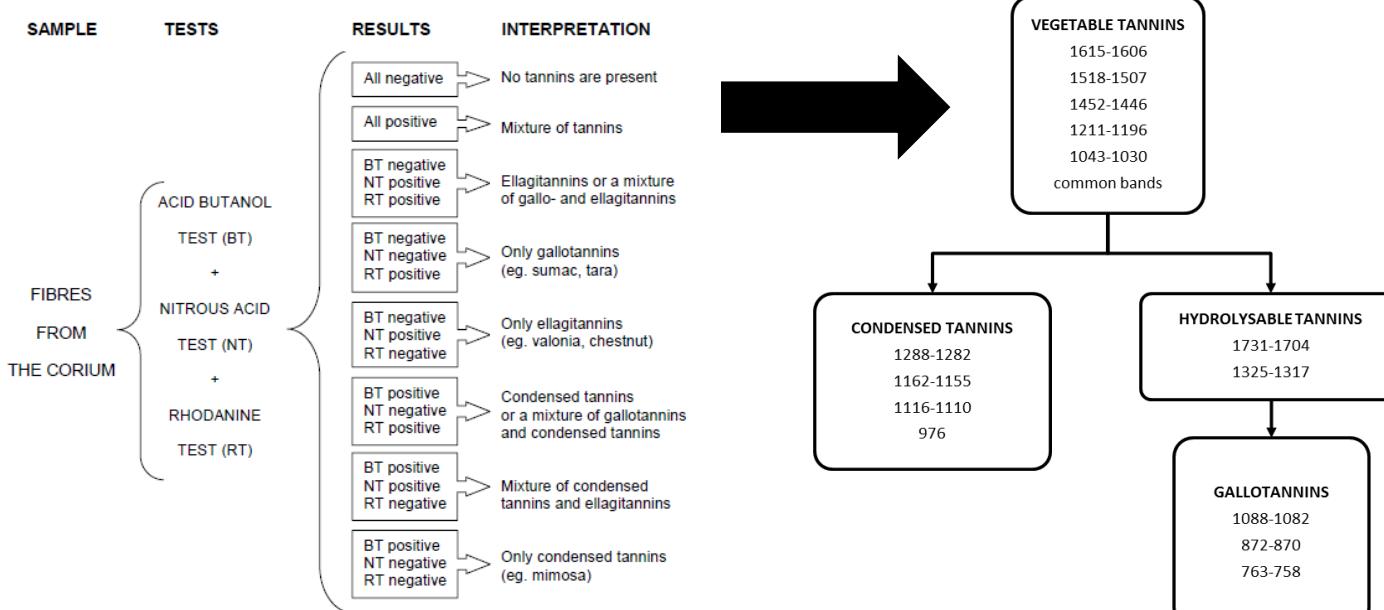
Book Chapter:

Rauter, A. P.; Xavier, N. M.; Lucas, S. D.; Santos M. , M. Malik; In: *Advances in Carbohydrate Chemistry and Biochemistry* (Ed. Derek Horton), Vol. 63, Burlington: Academic Press, 2010, pp 29-99

Applying Chemistry to Society | Studies on Material Cultural Heritage to Understand Our Past



History, materials and techniques of European decorative leathers produced between 1500 and 1800



Lina Falcão
PhD student



Maria Eduarda Araújo
Senior researcher

Publications:

- Lina Falcão, M. Eduarda M. Araújo, *Journal of Cultural Heritage*, 2011, 12, 149
Lina Falcão, M. Eduarda M. Araújo, *Journal of Cultural Heritage*, 2013, 14, 499
Lina Falcão, Maria Eduarda M. Araújo, *Vibrational Spectroscopy*, 2014, 74, 98

Collaboration:

