

The molecules of life

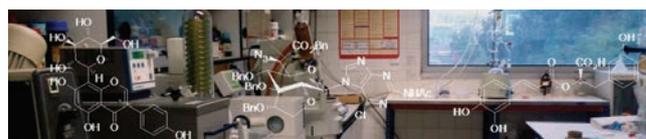
The Carbohydrate Chemistry Group on the contribution of sugars to health and nutrition

Carbohydrates are the most abundant biological molecules on Earth and are present in all living organisms. As renewable raw materials, they are economically viable and sustainable, allowing European economic growth without damaging the environment. Research in the Carbohydrate Chemistry Group on these ‘molecules of life’ is directed towards finding solutions to societal challenges underlying innovation, economic and social benefits. As a centre of excellence of the former ESF EUROGLYCOFORUM network, and integrating Portugal’s Centro de Química e Bioquímica, Faculdade de Ciências and Universidade de Lisboa (CQB-FCUL), and funded by Fundação para a Ciência e a Tecnologia, the Carbohydrate Chemistry Group offers creative approaches in glycochemistry for the understanding of complex biological and biochemical processes.

Sugars as sustainable raw materials for functional molecules towards disease prevention and control

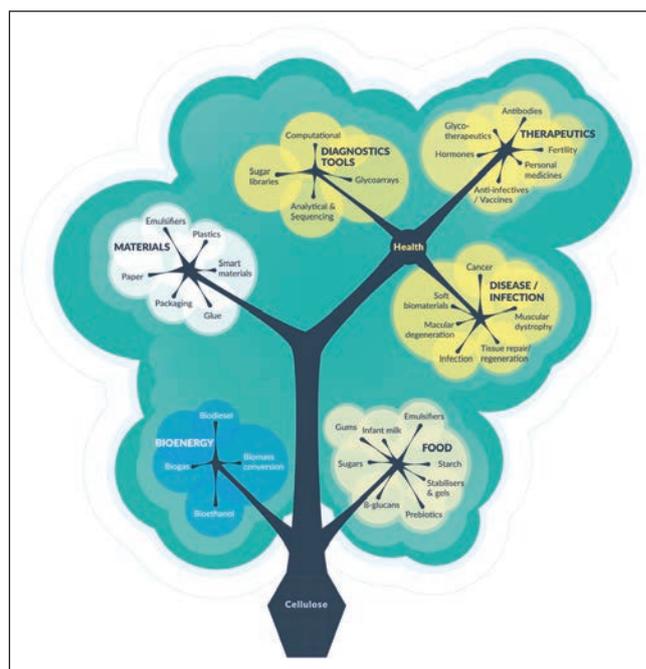
Within our goals, which focus on the chemistry for health and nutrition, we succeeded in developing new sugar-based antibiotics with new mechanisms of action to overcome antimicrobial resistance, with an added value for biosecurity purposes. The prevention of cognitive decline could also have a tremendous public health impact, and we have addressed this challenge by developing multi-target functional food ingredients that have demonstrated efficiency in controlling diabetes and in preventing cognitive impairments.

The latter are a hallmark of Alzheimer’s disease (AD), for which symptomatic treatment is mainly based on acetylcholinesterase (AChE) inhibitors. We have recognised a new binding site of this enzyme to a polyphenol, identified as a naturally occurring food ingredient with a potent anticholinergic activity, which was also active against amyloid aggregation and interacted with prion protein. These findings opened the way to the generation of compound libraries against this multifactorial disease, also



bridging polyphenols and sugars that are known to avoid amyloid peptide re-aggregation. Both AD and Type 2 diabetes share enhanced production and accumulation of β -amyloid peptide and abnormal levels of AChE and butyrylcholinesterase (BChE). Hence, selective inhibitors of each of both enzymes are required to unravel the role of BChE in both disease pathologies.

We were also able to generate a library of nucleosides that are potent and selective inhibitors either of BChE or of AChE, depending on structural requirements, well established by us, and developed procedures aiming at an easy access to such molecules. Within the project entitled ‘Diagnostic and Drug Discovery Initiative for Alzheimer’s Disease’, funded by the European Union’s Seventh Framework Programme for research, technological development and demonstration under grant agreement no 612347, we have the leadership of work package three covering the design, synthesis and testing of novel chemical entities. We are developing synthetic strategies and new biomolecular entities aiming at multi-target drug discovery against this devastating disease. This project is





co-ordinated by the University of Sheffield, UK, with the participation of the companies Eli Lilly (UK) and Biofrodug (Italy). New frameworks for nucleoside/nucleotide mimicry were also designed and synthetic approaches developed to access analogues/mimetics intended to inhibit other therapeutically relevant enzymes, namely cyclin-dependent kinases and carbonic anhydrases.

Supporting healthy living and healthy ageing

In the EU, the number of people aged 65+ is expected to increase from 85 million in 2008 to about 151 million in 2060. While longevity is a great achievement, it is also a challenge for public and private budgets, as well as for older people and their families. Innovation is required to retard frailty, playing a key role in ageing well. Our networking strategy and research encouraged the application in 2012 to membership of the European Innovation Partnership on Active and Healthy Ageing – Action Group 3 – on the prevention and early diagnosis of frailty and functional decline, both physical and cognitive, in older people (EIP-AHA A3) with the approved commitment entitled ‘Healthy ageing with innovative functional foods/leads for degenerative and metabolic diseases’ (INNOVAFUNAGEING).

Reinforcing our internationalisation with the newly formed consortium generated in this EIP-AHA A3 forum, and under our leadership, the Foundation of FCUL became a partner of the project entitled ‘PERSONALISED ICT supported Service for Independent Living and Active Ageing – PERSSILAA’, funded from the European Union’s Seventh Framework Programme – Information and Communication Technologies (FP7-ICT) under grant agreement number 610359. It is co-ordinated by the University of Twente (the Netherlands), and the additional

partners are the Universidad Politécnica de Madrid and the Fundació Privada Institut de Neurorehabilitació Guttman (Spain), Roessingh Research and Development BV (the Netherlands), University College Cork – National University of Ireland, Azienda Ospedaliera Universitaria Federico II and Nexera (Italy).

The goal of this project is to develop a new service module to screen for and prevent frailty in community dwelling older adults, integrating nutrition, physical and cognitive function and comprising remote service modules for screening, monitoring and training. With the leadership of the work package on nutrition, the Portuguese team members belong to CQB, to the Centro de Estatística e Aplicações (CEaUL) from FCUL Department of Statistics and to the National Health Institute Doutor Ricardo Jorge (INSA). Amongst our contributions to the project, the design and development of the NUTRIAGEING website (<http://nutriaging.fc.ul.pt/>) should be highlighted. By bridging nutritional science with culinary, functional food ingredients and vegetable gardens, this interactive website is a unique and easy to use tool for end users with the mission ‘Learn and Enjoy!’.

The left figure shows the NUTRIAGEING website and the Portuguese PERSSILAA team. Top to bottom: Amélia Pilar Rauter (leader, CQB-FCUL), António Ferreira (CQB-FCUL), Marta Sousa Silva (CQB-FCUL), Helena Soares Costa (INSA), and Kamil Feridun Turkman (CEaUL).



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