Amelia Pilar Rauter, J Glycobiol 2017, 6:2(Suppl)
DOI: 10.4172/2168-958X-C1-008

Exploiting polyphenols for Alzheimer's disease prevention: From nature to the lab

Amelia Pilar Rauter
Universidade de Lisboa, Portugal

Alzheimer's disease (AD) is a multifactorial pathology with unknown etiology and up to now, without cure. Solutions for early diagnosis and disease prevention are urgently needed. We present two case studies on the medicinal plants *Salvia sclareoides* and *Genista tenera*, the first one known for its effects on memory loss and the other one used to control diabetes, whose patients are at higher risk of developing AD than normal elderly. Methodologies are based on functional ingredient isolation and structure elucidation and synthesis, followed by the study of the mechanisms of action. The biological properties of *S. sclareoides* demonstrated that extracts are potent inhibitors of acetylcholinesterase (AChE), the enzyme degrading the neurotransmitter acetylcholine, whose inhibition is used to treat AD patients in early disease stages. Rosmarinic acid was identified as plant major component and a new binding site of AChE for this constituent was discovered, opening the way to new strategies for lead development. It was demonstrated that plant extracts prevent normal Prion protein to convert to Prion infectious isoform and interact with AD toxic oligomers, removing amyloid fibrils to form amorphous aggregates. These findings clearly reinforce the potential of the plant to act on both amyloid and cholinergic events for AD prevention. Also diabetes is an amyloid disease and the scientific background of the traditional use of *G. tenera* has been unraveled. The active principles were mainly O- and C-glycosyl polyphenols, namely the potent antihyperglycemic 8-glucosylgenistein. This discovery has encouraged the generation of a library of compounds structurally based on its precursors and analogues and some of them demonstrated a potent anti-diabetic activity. The multiple mechanisms of action of the polyphenols studied were identified. α-glucosidase and glucose-6-phosphatase inhibitory activity was shown by the polyphenols that also demonstrated UV cellular damaging protection and antioxidant activity, maintained after *in vitro* digestion with artificial gastric and pancreatic juices. Dihydrochalcones demonstrated a selective and potent inhibition of sodium glucose co-transporter-2. Interestingly, suppression of islet amyloid polypeptide (IAPP) fibril formation was produced by 8-glucosylgenistein. Molecular recognition studies with IAPP and $A\beta_{1-42}$ confirmed the same binding mode for both amyloid peptides, supporting this molecular entity for intervention in amyloid events of both diabetes and the frequently associated Alzheimer's disease. C-glucosylation has also proven to efficiently increase the anti-diabetic activity of the polyphenols studied and to prevent their behavior as PAINS (Pan-Assay Interference compounds).

Biography

Amelia Pilar Rauter has her expertise in biomolecular and medicinal chemistry focusing on disease prevention. Leader of the European Innovation Partnership FCUL consortium at the A3 group for disease prevention, and Secretary of the European Carbohydrate Organization and of the IUPAC Division (III) on Organic and Biomolecular Chemistry, she has dedicated her research to the innovation on functional ingredients for AD prevention by bridging nature with sustainable chemistry.

aprauter@fc.ul.pt

Notes: