Plant-derived extracts against neurodegenerative disorders: an integrated workflow to characterize their anti-amyloidogenic properties

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Abstract:

The prevalence of neurodegenerative disorders (NDs) is expected to rise with the increasing life expectancy worldwide. In this context, amyloid aggregation is a shared hallmark of several NDs such as Alzheimer's disease (AD), Parkinson's disease (PD) and spino-cerebellar ataxia (SCA). The aggregated species, in particular oligomers, exert neurotoxic effects which can lead to loss of synaptic function and cell death.[1]

While no resolutive treatments are available, preventive strategies, which inhibit the formation of pre-fibrillar species, are needed. In this context, plant-derived extracts (PDEs) are historically known to have beneficial effects towards human's health and are a rich source of bioactive compounds. Among those, polyphenols are a class of secondary metabolites characterized by different bioactive properties, such as radical-scavenging, antimicrobial, anti-inflammatory and antitumor activity.[2,3]

In order to characterize the metabolic profile of PDEs, Nuclear Magnetic Resonance (NMR) spectroscopy together with High-Resolution Mass Spectrometry (HR-MS) are employed. Moreover, to identify bioactive metabolites, PDEs are tested for their anti-amyloidogenic properties on different amyloid peptides and proteins, including amyloid-β, α-synuclein and ataxin-3. To evaluate their role in amyloid aggregation inhibition, Thioflavin T (ThT) assay can be employed to screen PDEs for active compounds, while Saturation Transfer Difference (STD) NMR comes as a tool for the detection of extract-protein interactions and for the identification of binding epitopes.[4]

Together with other structural and biophysical techniques, such as Infrared Spectroscopy (IR), Atomic Force Microscopy (AFM) and Circular Dichroism (CD), it is possible to further understand the mechanisms of inhibition of protein aggregation and structural changes in fibril morphology, thus making PDEs useful in NDs prevention.

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