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Potential of Polyphenols from Tamarix Gallica towards Common Pathological Features of Diabetes and Alzheimer's Diseases

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Abstract : Type 2 diabetes mellitus (T2DM) and Alzheimer's disease (AD) are characterized as a peripheral metabolic disorder and a degenerative disease of the central nervous system, respectively. It is now widely recognized that T2DM and AD share many pathophysiological features including glucose metabolism, increased oxidative stress and amyloid aggregation. Amyloid beta (Aβ) is the components of the amyloid deposits in the AD brain and while the component of the amyloidogenic peptide deposit in the pancreatic islets of Langerhans is identified as human islet amyloid polypeptide (hIAPP). These two proteins are originated from the amyloid precursor protein and have a high sequence similarity. Although the amino acid sequences of amyloidogenic proteins are diverse, they all adopt a similar structure in aggregates called cross-beta-spine. Add at that, extensive studies in the past years have found that like Aβ1-42, IAPP forms early intermediate assemblies as spherical oligomers, implicating that these oligomers possess a common folding pattern or conformation. These similarities can be used in the search for effective pharmacotherapy for DM, since potent therapeutic agents such as antioxidants with a catechol moiety, proved to inhibit Aβ aggregation, may play a key role in the inhibit the aggregation of hIAPP treatment of patients with DM. Tamarix gallica is one of the halophyte species having a powerful antioxidant system. Although it was traditionally used for the treatment of various liver metabolic disorders, there is no report about the use of this plant for the treatment or prevention of T2DM and AD. Therefore, the aim of this work is to investigate their protective effect towards T2DM and AD by isolation and identification of α-glucosidase inhibitors, with antioxidant potential, that play an important role in the glucose metabolism in diabetic patient, as well as, the polymerization of hIAPP and Aβ aggregation inhibitors. Structure-activity relationship study was conducted for both assays. And as for α-glucosidase inhibitors, their mechanism of action and their synergistic potential when applied with a very low concentration of acarbose were also suggesting that they can be used not only as α-glucosidase inhibitors but also be combined with established α-glucosidase inhibitors to reduce their adverse effect. The antioxidant potential of the purified substances was evaluated by DPPH and SOD assays. Th-T assay using 42-mer amyloid β-protein (Aβ42) for AD and hIAPP which is a 37-residue peptide secreted by the pancreatic β –cells for T2DM and Transmission electronic microscopy (TEM) were conducted to evaluate the amyloid aggragation of the actives substances. For α-glucosidase, p-NPG and glucose oxidase assays were performed for determining the inhibition potential and structure-activity relationship study. The Enzyme kinetic protocol was used to study the mechanism of action. From this research, it was concluded that polyphenols playing a role in the glucose metabolism and oxidative stress can also inhibit the amyloid aggregation, and that substances with a catechol and glucuronide moieties inhibiting amyloid-β aggregation, might be used to inhibit the aggregation of hIAPP.

Keywords : α-glucosidase inhibitors, amyloid aggregation inhibition, mechanism of action, polyphenols, structure activity relationship, synergistic potential, tamarix gallica
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