Neuroprotective effects of 7-tetrahydroxyflavone against Alzheimer's disease through Hypothalamic-Pituitary-Adrenal Axis and Nrf2 linked bidirectional pathways

undamental Research Grant Schem

Alzheimer's disease is an age-related memory loss that affects cognitive function. In Alzheimer's type of dementia, stress escalates the acetylcholinesterase enzyme with accumulation of amyloid peptide which eventually causes declining cognition, emotion, and social health. Worldwide 46.8 million people are living with dementia and in Malaysia was 123,000 people in 2015 and projected to 261,000 by 2030 and to 590,000 in 2050. National health and morbidity survey-senior health of Malaysia, 2018 states the prevalence is 8.6%. In Malaysia, according to Alzheimer's disease International, the prevalence of dementia was 123,000 people during 2015. As per Alzheimer's disease foundation, the number was projected to be 261,000 by 2030 and will continue to increase to 590,000 people in 2050. It's also denoted that in Malaysia 8.6% of elderly population prevails with dementia with its rapid growth and morbidity, it ranks second on the burden of disease in Asia Pacific Region. Currently, there is a worldwide effort to find better ways to treat the disease, delay its onset, and prevent it from developing.

As a preventive measures' basic quality of life enhancements with nutritious food habits balanced with fruits and natural products value adds to neuroprotection. At present there is no cure for Alzheimer's disease. Despite symptomatic treatments, any drugs or any chemical entity which controls the disease progression value adds the therapeutic management of AD and makes life better for the millions of people living with Alzheimer's Disease. Current Alzheimer's treatment, acetylcholinesterase enzyme prevents Alzheimer's from progressing and it can temporarily reduce the dementia symptoms. Despite the low bioavailability profile, the currently available drugs such as AChE inhibitors (Donepezil, Tacrine & Rivastigmine) are only affording symptomatic control and effects. A new novel drug Aducanumab was recently approved. However, these drugs also alter the brain neurotransmitters and cause adverse effects such as insomnia, altered mental status, anorexia, visual disturbances, muscle cramps and asthenia.

Polyphenolic compounds and flavonoids have abundant neuroprotective and antioxidant potential to be elucidated and optimized as formulation delivery to the brain which renders neuroprotection through delaying and preventing the AD without adverse effect. The study was aimed to envisage the regulation of neuroimmune and neuroendocrine coordination through nuclear factor erythroid 2–related factor 2 (Nrf2) pathway for organic brain balance. The optimized formulation of polyphenolic drugs was predicted to exhibit the neuroprotective effect with enhanced bioavailability for treating early onset AD (EOAD), Late onset AD (LOAD) and benefits geriatric care for national action plan for dementia, promote mental health and wellness and expands new drug development.



Our team members, from the Faculty of Pharmacy, UiTM are investigating the neuroprotective molecular targets where polyphenolic 7-tetrahydroxyflavone interacts in the brain. This research explores the knowledge on novel theories of neuroimmune and neuroendocrine bidirectional pathways for treating AD.

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