Literature review

Alzheimer's disease (AD) is a neurodegenerative disorder pathologically characterised by the progressive damage and/ or destruction of nerve cells (neurons) within the brain. While early stage AD is invariably linked to the onset of dementia, a syndrome affecting memory, language and cognitive skills, late stage AD patients become severely debilitated and require around-the-clock care. Although there are currently a number of drugs available on the market to delay the onset of AD, these are often quite expensive and often leads to patients experiencing side effects such as nausea, dizziness and muscle weakness. There are several proposed mechanisms relating to the biochemical neuropathology of AD, which most notably include; the hyperphosphorylation of tau proteins, the development of amyloid beta ($A\beta$) plaques and the reduction of intercellular acetylcholine (ACh) concentrations.

Functional foods is an area of natural product research that largely compliments the ethnopharmacological basis of drug discovery but differs from the latter in the fact that they are not consumed in high doses like drugs (e.g. tablets, aerosols or intravenously) but rather as part of everyday nutrition. In this project, crude extracts of known edible medicinal sources will serve as basis for further study in this project. The mining of natural products provides a real opportunity to discover novel molecules that may have the potential to function as either drugs to delay the progression of AD neurodegeneration or alternatively function as part of everyday nutrition to protect against the onset of AD itself.

Objectives

The main objectives of this project are;

I. To carry out a detailed investigation of edible plants already demonstrating significant potential (in preliminary pilot studies) to reduce the effects of Alzheimer's symptoms, as well as screening a library of edible Irish natural product extracts housed at IT Sligo, for significant anti-AD activity.

II. To carry out bioactivity-guided fractionation of up-scaled anti-AD extracts, using a range of separation and chromatographic technologies, to generate fractions with enriched anti-AD activity.

III. Measure the efficacy of enriched anti-AD activity fractions to potentiate an inhibitory response against BACE1 activity as well as modulate the impact of AD within specific neuroblastoma cell lines.

IV. Purify and chemically identify novel compounds that could be exploited as novel treatments for the symptoms of AD.

Person Specification:

The ideal candidate will demonstrate the appropriate mix of knowledge, experience, skills, talent and abilities as outlined below:

Knowledge and Experience:

- Ability to manage and conduct a specific programme of research under the leadership of the main supervisor and external supervisor (essential).
- A strong analytical background with a BSc (2:1 minimum) in analytical, bioanalytical chemistry, Biomedical or a relevant related discipline from an approved degree awarding institution (essential).
- A strong understanding, interest and demonstrated practical experience in the following; Chromatographic techniques and Biological assays.

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