

Maple syrup extract inhibits the beta-amyloid and tau oligomerization of Alzheimer's disease Donald F. Weaver^{1,3}, donald.weaver@uhnres.utoronto.ca, Cassandra Hawco^{1,3}, Yan- Fei Wang^{2,3}, Marcia Taylor^{2,3}. (1) Chemistry, Toronto Western Research Inst., Toronto, Canada (2) Biology, Toronto Western Research inst., Toronto, Canada (3) Univ. of Toronto, Canada

Alzheimer's disease (AD) is the most common type of dementia, arising from oligomerization of beta-amyloid (Abeta) and tau peptides; there are no disease stabilizing drugs for the treatment of AD. Since several natural products (resveratrol, ferulate) have anti-oligomeric properties, we sought to identify novel plant products with potential anti-AD efficacy. During our systematic search for natural product-based anti- protein misfolding agents for the putative treatment of AD, we investigated maple syrup. Maple syrup is produced by thermal evaporation of the sap from maple (Acer) trees, a process which concentrates the contained sugars as well as producing a variety of chemical reactions responsible for the distinct taste of the syrup. In addition to sugars, the collected sap contains a wide range of oligosaccharides, amino acids, polyphenols and phytohormones. Three separate extracts of maple syrup were sequentially isolated: Extract A – ethyl acetate soluble; Extract B – n-butanol soluble, methanol insoluble; Extract C – n-butanol soluble, methanol soluble. Each of these three extracts was then evaluated for anti-protein misfolding activity in three separate assays: [i] biotinylated Abeta ELISA-based anti-oligomerization assay, [ii] Abeta thioflavin T anti-aggregation assay (ThT), and [iii] tau thioflavin S anti-aggregation assay (ThS). Extract A demonstrated significant Abeta anti-oligomeric and Abeta anti-aggregant activities as well as the ability to prevent tau aggregation. Extract A inhibited Abeta aggregation by 47% at 100 microM, and demonstrated concentration-dependent activity in the ThT assay. Extracts B and C did not exhibit any activity. This trend was also demonstrated in the Abeta oligomerization assay with A demonstrating significant activity, while both Extracts B and C showed no difference from control ($p = 0.05$). Extract A also prevented aggregation of tau by 41% at 100 microM; extracts B and C had no activity in the ThS aggregation assay. Thus, an ethyl acetate extract of maple syrup has significant Abeta/tau anti-oligomerization activity. This implications of this finding and the potential role of food products not only as therapeutics, but also as confounding variables in clinical trial design for AD will be considered.