Journal of Alzheimer's Disease 31 (2012) 879–889
DOI 10.3233/JAD-2012-120229
IOS Press

Synaptic Silencing and Plasma Membrane Dyshomeostasis Induced by Amyloid-β Peptide are Prevented by *Aristotelia chilensis* Enriched Extract

Jorge Fuentealba[a,*], Andrea Dibarrart[a], Francisco Saez-Orellana[a], María Cecilia Fuentes-Fuentes[a], Carlos N. Oyanedel[a], José Leonardo Guzmán[c], Claudia Perez[d], José Becerra[d] and Luis G. Aguayo[b]
[a]*Laboratorio de Screening de Compuestos Neuroactivos, Universidad de Concepción, Concepción, Chile*
[b]*Laboratorio de Neurofisiología, Universidad de Concepción, Concepción, Chile*
[c]*Laboratorio de Neurofisiología molecular, Departamento de Fisiología, Facultad de Cs. Biologicas, Universidad de Concepción, Concepción, Chile*
[d]*Laboratorio de Productos Naturales, Departamento de Botánica, Fac. De Cs. Naturales y Oceanográficas, Universidad de Concepción, Concepción, Chile*

Accepted 19 May 2012

Abstract. Alzheimer's disease (AD) is characterized by the presence of different types of extracellular and neurotoxic aggregates of amyloid-β (Aβ). Recently, bioactive compounds extracted from natural sources showing neuroprotective properties have become of interest in brain neurodegeneration. We have purified, characterized, and evaluated the protective potential of one extract enriched in polyphenols obtained from *Aristotelia chilensis* (MQ), a Chilean berry fruit, in neuronal models of AD induced by soluble oligomers of $A\beta_{1\text{-}40}$. For example, using primary hippocampal cultures from rats (E18), we observed neuroprotection when the neurons were co-incubated with Aβ (0.5 μM) plus MQ for 24 h (Aβ = 23 ± 2%; Aβ + MQ = 3 ± 1%; $n = 3$). In parallel, co-incubation of Aβ with MQ recovered the frequency of Ca^{2+} transient oscillations when compared to neurons treated with Aβ alone (Aβ = 72 ± 3%; Aβ + MQ = 86 ± 2%; $n = 5$), correlating with the changes observed in spontaneous synaptic activity. Additionally, MAP-2 immunostaining showed a preservation of the dendritic tree, suggesting that the toxic effect of Aβ is prevented in the presence of MQ. A new complex mechanism is proposed by which MQ induces neuroprotective effects including antioxidant properties, modulation of cell survival pathways, and/or direct interaction with the Aβ aggregates. Our results suggest that MQ induces changes in the aggregation kinetics of Aβ producing variations in the nucleation phase (Aβ: $k_1 = 2.7 \pm 0.4 \times 10^{-3}$ s^{-1} MQ: $k_1 = 8.3 \pm 0.6 \times 10^{-3}$ s^{-1}) and altering Thioflavin T insertion in β-sheets. In conclusion, MQ induces a potent neuroprotection by direct interaction with the Aβ aggregates, generating far less toxic species and in this way protecting the neuronal network.

Keywords: Alzheimer's disease, amyloid-β peptide, antioxidant, hippocampal neurons, maqui, nutraceuticals, polyphenols

INTRODUCTION

Alzheimer's disease (AD) is a complex and progressive clinical condition where the main consequences are related to cognitive and memory dysfunctions [1, 2] due to irreversible neurodegeneration, synaptic dysfunction, and neuronal death. This pathology is one

*Correspondence to: Dr. Jorge Fuentealba Arcos, PhD, Laboratory of Neuroactive Compound Screening, Faculty of Biological Sciences, Department of Physiology, PO Box 160-C, University of Concepcion, Barrio Universitario s/n, Concepcion, Chile. Tel.: +56 41 2661082; Fax: +56 41 2204557; E-mail: jorgefuentealba@udec.cl.

ISSN 1387-2877/12/$27.50