

EVIDENCE FOR PEA ANTIINFLAMMATORY PROPERTIES IN A β CHALLENGED C6 RAT GLIOMA CELLS

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There is increasing evidence that neuroinflammation driven by abnormal or prolonged glial activation contributes to pathogenesis and progression of disorders such as Alzheimer’s disease (AD). Amyloid beta (A β) induced stress may result in increased levels of inflammatory molecules produced by chronically activated glia, leading to neuron damage, provoking further glial activation, and resulting in a detrimental cycle of neuroinflammation and neurodegeneration. Targeting glial activation pathways may then result in attenuation of neuronal pathology and cognitive function deficits.

Palmitoylethanolamide (PEA) belongs to the family of “endocannabinoid-like” derivatives, so called because they exhibit cannabimimetic properties but are devoid of direct affinity for the CB receptors *in vitro*. As it is produced during inflammation, it was proposed to act as an ALIAmide (Autacoid Local Inflammation Antagonist Amide).

Numerous studies have shown PEA to perform a wide range of pharmacological actions including analgesic, anti-inflammatory, anticonvulsant and antiproliferative effects, although molecular mechanisms underlying these properties are still a matter of speculation.

The present study was aimed to investigate *in vitro* the role of PEA in the modulation of inflammatory response in A β challenged C6 rat glioma cells.

To this purpose, C6 cells were cultured in 10% FCS supplemented DMEM and treated with 1 μ g/ml of A β (1–42) in the presence or absence of PEA, at concentrations ranging from 10⁻⁸ to 10⁻⁶ M.

24 h after A β challenge NO was measured as nitrite (NO²⁻) released in cell supernatant by a spectrophotometer assay based on the Griess reaction, while lysed cells subsequently underwent Western Blot analysis with anti-iNOS and anti-p38 MAPK antibodies respectively. In the same experimental conditions, Electro Mobility Shift Assay (EMSA) was employed to evaluate NF- κ B and AP-1 transcription factors activation.

Obtained results indicated that PEA (10⁻⁸ to 10⁻⁶ M) concentration-dependently reduced iNOS protein expression (-30 \pm 2 %, - 52 \pm 6 %, - 77 \pm 4 % respectively) and NO release (- 28.7 \pm 3.2 %, - 48 \pm 5 %, -68 \pm 3.5 % respectively) in C6 cells following A β challenge. Parallel data showed that PEA (10⁻⁷ and 10⁻⁶ M), acting as p38-MAP kinase phosphorylation inhibitor, significantly reduced both NF- κ B (- 30 \pm 3.1 %, - 56 \pm 6 % respectively) and AP-1 (- 27 \pm 2 %, -72 \pm 4.7 % respectively) activation due to A β exposure.

This evidence overall indicates that PEA can be able to exert *in vitro* a significant anti-inflammatory effect in A β stimulated astroglia, prospecting this compound as a useful tool in the attenuation of A β induced neuroinflammation.