Cytokines down regulation is involved in the protective effect of Bergamot juice extract in β-amlyloid-stimulated THP-1-cells

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Several evidence demonstrated that mechanisms responsible for transduction and amplification of inflammatory responses contribute to the production of neurotoxic mediators in neurodegeneration. A characteristic feature of chronic inflamed tissues is the presence of an increased number of monocytes, as well as monocyte-derived tissue macrophages, that can be referred to microglia cells in the central nervous system (CNS). Noteworthy amyloid-beta (Aβ) peptide drives cerebral neuroinflammation by activating microglia and astrocytes promoting the expression of inflammatory cytokines, the activation of the complement cascade, and the induction of inflammatory enzyme systems. Several natural compound including antioxidants have been reported to protect against Aβ-induced neurotoxicity in cultured cell systems, however further effects should be evaluated.

Citrus bergamia Risso et Poiteau (Bergamot) is a small tree cultivated almost exclusively along the southern coast of Calabria region (Italy). Bergamot fruit is used mostly for the extraction of its essential oil widely used in perfume industry, while bergamot juice is considered just a secondary and discarded product.

This study was designed to evaluate the effect of a bergamot juice extract (BJe) against Aβ-induced neuroinflammation process. To this aim, experiments were performed on human monocytic THP-1 cells, a useful model of human monocytes/macrophages, widely used in *in vitro* neurodegeneration research.

Identification and quantification of the flavonoids content in BJe used in this study was attained by means of RP-HPLC in combination with UV and MS detectors.

Exposure of THP-1 cells for 24 hs to Aβ 1-42 (500 nM) or BJe (in a range of 0.05-0.1 mg/ml) did not produce significant changes in cell viability, as assessed by MTT test. Incubation of THP-1 cells with Aβ significantly increased the expression of both IL-6 and IL-1β as demonstrated by Real-Time PCR evaluation of mRNA transcripts and ELISA assay. One hs incubation of THP-1 cells with 0.1 mg/ml BJe reduced both IL-6 and IL-1β levels by about 60% and 40% respectively.

Considering that monocytes play a relevant role in neurodegenerative disease contributing to the inflammatory process, these preliminary data provide evidence that BJe could be effective to reduce neuroinflammation caused by fibrillar Aβ peptides in monocyte/microglial cells.

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