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A promising Neuroprotective Agent for the Treatment of Multiple Sclerosis: 3-beta-Hydroxyolean-12-en-28-oate İsolated from *Capparis ovata*

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Aim of the study: Multiple sclerosis (MS) is a chronic autoimmune disease where the inflammation throughout CNS cause demyelinated plaques of gliotic scar tissue and a variable degree of axonal loss. There is still no complete cure for MS without undesired side effects. Thus, studies on medicinal plants have been pulling in much consideration due to their potential constituents applicable to modern medicine. In this study, potential anti-inflammatory and immunomodulatory activities of Oleanolate (OA, 3β-hydroxyolean-12-en-28-oate), a universal pentacyclic multifunctional triterpenoid, isolated from *Capparis ovata*were investigated in SH-SY5Y neuroblastoma cells.

Material and Methods:*Capparis ovata* parts had been collected from the beginning of May to end of September in Denizli and Burdur in 2012. (PAMUH 2012000006300). Preparation of water extract of Capparis ovata (COWE) parts are defined elsewhere in detail (Turkish Patent Institute TR 2012 04093B). Oleanolate was isolatedfrom the COWE by dichloromethane sub-extraction and was identified by TLC, NMR, and MS analysis. OA was applied at non-toxic doses to the human neuroblastoma cell line SH-SY5Y to study the regulation of the expression of MS-related genes. Total RNA from SH-SY5Y was isolated using RNeasy Plus Universal Mini Kit. RNA was reversely transcribed using Easy Script cDNA Synthesis Kit. Custom designed, tested and validated human MS primers along with the housekeeping genes were used for quantitative determination of differential gene expression profiles between different treatment groups. Then synthesized cDNA was used for qPCR protocol. PCR Array Data Analysis Web Portal was applied for calculations of folds changes in mRNA abundance accordingly to the $2^{-\Delta\Delta Ct}$ method.

Results: The results are the average of the experiments conducted in three independent set of experiments. Statistically significant changes in the expression of 13 genes were detected. The altered expression was observed in genes belonging to myelination, T-cell activation/signaling, adaptive immunity, inflammation regulation, apoptosis, cell adhesion, cellular stress, receptors, and transcription factors. These genes have been suggested to be involved in the development of MS. The expressions of pro- and anti-inflammatory chemokines/cytokines such as CXCL9, CXC10, and have been shown to be prominently reduced with OA treatment. Also, expressions of TNF and C1S were also downregulatedwith OA in these cells. Thus, these data strongly suggest that OA is a potent inhibitor of the T cell activation and differentiation. The expression of MMP9, which is known to be important in leucocyte infiltration was also significantly decreased with OA treatment. It was also found out that the transcripts levels of myelin-specific proteins such as MAG and PLP1were upregulated by OA. Therefore, it-9 may be more beneficial in remyelination of demyelinated axons in MS. Collectively, these results indicate that OA was associated with the suppression of molecules essential for disease development and induction of molecules important in healing.

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Keywords: 3-beta-Hydroxyolean-12-en-28-oate, Multiple sclerosis, *Capparis ovata* SH-SY5Y, Anti-inflammatory, Neuroprotective.