Triptolide

Triptolide is a principal diterpene triepoxide from the Chinese medical plant Tripterygium wilfordii Hook. f., whose extracts have been utilized in dealing with diverse diseases in traditional Chinese medicine for centuries.

Triptolide inhibit the proliferation of glioma cells in vitro, which is associated with promoting the expression of Bax and inhibiting the expression of Bcl-2 and accelerating cell apotosis [1)].

Findings suggest that TP inhibits the growth of immortalized HT22 hippocampal cells via persistent ERK-1/2 activation by suppressing MKP-1 expression. Additionally, a study provides evidence supporting that MKP-1 may play an important role in regulation of neuronal cell growth [2)].

Results demonstrated that triptolide was capable of promoting peripheral nerve regeneration. Additionally, triptolide significantly decreased the levels of pro-inflammatory cytokines within injured nerves. These findings indicate the possibility of developing triptolide as a therapeutic agent for PNI. The neuroprotective effects of triptolide might be associated with its anti-inflammatory properties [3)].

Sai et al. explored the interaction of TPL and TMZ in glioma-initiating cells (GICs) and the potential mechanism. A GIC line (GIC-1) was successfully established. Cell viability of GIC-1 after treatment was measured using a CCK-8 assay. The interaction between TPL and TMZ was calculated from Chou-Talalay equations and isobologram. Self-renewal was evaluated with tumor sphere formation assay. Apoptosis was assessed with flow cytometry and western blot. Luciferase assay was employed to measure NF-κB transcriptional activity. The expression of NF-κB downstream genes, NF-κB nuclear translocalization and phoshorylation of IκBα and p65 were evaluated using western blot. We found that GIC-1 cells were resistant to TMZ, with the expected IC50 of 705.7 μmol/L. Co-treatment with TPL yielded a more than three-fold dose reduction of TMZ. TPL significantly increased the percentage of apoptotic cells and suppressed the tumor sphere formation when combined with TMZ. Phosphorylation of IκBα and p65 coupled with NF-κB nuclear translocalization were notably inhibited after a combined treatment. Co-incubation synergistically repressed NF-κB transcriptional activity and downstream gene expression. TPL sensitizes GICs to TMZ by synergistically enhancing apoptosis, which is likely resulting from the augmented repression of NF-κB signaling. TPL is therefore a potential chemosensitizer in the treatment of GBM [4)].

Results demonstrated that triptolide inhibited cell viability and colony number of AtT20 cells in a dose- and time-dependent pattern. Triptolide also suppressed proopiomelanocortin (Pomc) mRNA expression and extracellular adrenocorticotropic hormone (ACTH) secretion in AtT20 cells. Flow cytometry prompted that triptolide leaded to G2/M phase arrest, apoptosis program and mitochondrial membrane depolarization in AtT20 cells. Moreover, dose-dependent activation of caspase-3 and decreased Bcl2/Bax proportion were observed after triptolide treatment. By western blot analysis we found that triptolide impeded phosphorylation of NF-κB p65 subunit and extracellular signal-regulated kinase (ERK), along with reduction of cyclin D1, without any impact on other NF-κB related protein expression like total p65, p50, IκB-α, p-IκB-α. Furthermore, the mouse xenograft model revealed the inhibition of tumor growth and hormone secretion after triptolide administration.

Altogether this compound might be a potential pharmaceutical choice in managing Cushing's disease [5].

1)
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