Corosolic acid

Corosolic acid is a pentacyclic triterpene acid found in Lagerstroemia speciosa. It is similar in structure to ursolic acid, differing only in the fact that it has a 2-alpha-hydroxy attachment.

Zhang et al. investigated the potential benefits of corosolic acid (CA) in the treatment of brain injury caused by ischemia/reperfusion (I/R) in adult male Sprague-Dawley rats. Injury occurs after a 2-hour transient occlusion of the posterior cerebral artery and subsequent reperfusion (after 20 hours). Furthermore, the experiment assessed the size of the infarct, the amount of brain water present, as well as the neurofunctional conditions in rats. In the study, several markers of inflammation and cytokines associated with brain injury were measured. The Elisa kit was used in this study to measure the mRNA expression of interleukin-6 (IL-6), interleukin-10 (IL-10), interleukin 1β, TNF-α (tumor necrosis factor), cyclooxygenase-2 (COX-2), prostaglandin E2 (PGE2), and nitrous oxide (NO). The CA treatment significantly reduced brain water content, brain infarction volume, neurological scores, and Evans blue leakage ($p < 0.001$ and $p < 0.001$). Experimental rats were treated with CA after a significantly reduced level of anti-inflammatory, pro-inflammatory, and oxidative stress mediators was noted in their body tissues and serum ($p < 0.001$). By suppressing inflammatory responses in rats, CA demonstrated anti-inflammatory and neuroprotective properties [1)]

Findings showed that CA ≤ 20 μM did not affect cell viability and cell proliferative rate of normal astrocyte and four GBM cells. Notably, 10 or 20 μM CA significantly inhibited cell migration and invasion of three GBM cells, decreased the protein level of F-actin and disrupted F-actin polymerization in these GBM cells. Further investigation revealed that CA decreased AXL level by promoting ubiquitin-mediated proteasome degradation and upregulating the carboxyl terminus of Hsc70-interacting protein (CHIP), an inducer of AXL polyubiquitination. CHIP knock-down restored the CA-reduced AXL and invasiveness of GBM cells. Additionally, we observed that CA-reduced Growth arrest-specific protein 6 (GAS6) and inhibited JAK2/MEK/ERK activation, and GAS6 pre-treatment restored attenuated JAK2/MEK/ERK activation and invasiveness of GBM cells. Furthermore, molecular docking analysis revealed that CA might bind to GAS6 and AXL. These findings collectively indicate that CA attenuates the invasiveness of GBM cells, attributing to CHIP upregulation and binding to GAS6 and AXL and subsequently promoting AXL degradation and downregulating GAS6-mediated JAK2/MEK/ERK cascade. Conclusively, this suggests that CA has potential anti-metastatic activity on GBM cells by targeting the CHIP/GAS6/AXL axis [2)].

1)
Zhang L, Sui S, Wang S, Sun J. Neuroprotective Effect of Corosolic Acid Against Cerebral Ischemia-Reperfusion Injury in Experimental Rats. J Oleo Sci. 2022 Sep 9. doi: 10.5650/jos.ess22130. Epub ahead of print. PMID: 36089398.
2)
Sun LW, Kao SH, Yang SF, Jhang SW, Lin YC, Chen CM, Hsieh YH. Corosolic Acid Attenuates the Invasiveness of Glioblastoma Cells by Promoting CHIP-Mediated AXL Degradation and Inhibiting GAS6/AXL/JAK Axis. Cells. 2021 Oct 28;10(11):2919. doi: 10.3390/cells10112919. PMID: 34831142; PMCID: PMC8616539.