Isorhapontigenin

Isorhapontigenin is a tetrahydroxylated stilbenoid with a methoxy group. It is an isomer of rhapontigenin and an analog of resveratrol.

It is found in the Chinese herb Gnetum cleistostachyum, in Gnetum parvifolium and in the seeds of the palm Aiphanes aculeata.

An isorhapontigenin tetramer, gnetuhainin R, can be isolated from the lianas of Gnetum hainanense.

Isorhapontin, the isorhapontigenin glucoside, can be found in spruce species such as the Norway spruce (Picea abies), the sitka spruce (Picea sitchensis) and the white spruce (Picea glauca).

A study of Xue et al. from the Department of Neurosurgery in the People's Liberation Army General Hospital, aimed to investigate the antioxidant effects of ISO on cerebral ischemia-reperfusion injury and its possible molecular mechanisms.

Focal cerebral ischemia-reperfusion injury (MCAO/R) model and primary cortical neurons were established an oxygen-glucose deprivation (OGD / R) injury model. After 24 hr of reperfusion, the neurological deficits of the rats were analyzed and hematoxylin and eosin stain was performed, and the infarct volume was calculated by TTC staining. In addition, the reactive oxygen species (ROS) in rat brain tissue, the content of 4-Hydroxynonenal (4-HNE), and 8-hydroxy2deoxyguanosine (8-OHdG) were detected. Neuronal cell viability was determined by MTT assay. Western blot analysis was determined for protein expression.

ISO treatment significantly improved neurological scores, reduced infarct volume, necrotic neurons, ROS production, 4-HNE, and 8-OHdG levels. At the same time, ISO significantly increased the expression of Nrf2 and HO-1. The neuroprotective effects of ISO can be eliminated by knocking down Nrf2 and HO-1. In addition, knockdown of the PKCε blocked ISO-induced nuclear Nfr2, HO-1 expression.

ISO protected against oxidative damage induced by brain I/R, and its neuroprotective mechanism may be related to the PKCε/Nrf2/HO-1 pathway [1)]

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investigated the potential inhibitory effect of isorhapontigenin (ISO), an anticancer compound identified in our recent investigations, on anchorage-independent growth of patient-derived glioblastoma spheres (PDGS) and its mechanism of action.

Results: ISO treatment resulted in significant anchorage-independent growth inhibition, accompanied with cell cycle G0-G1 arrest and cyclin D1 protein downregulation in PDGS. Further studies established that cyclin D1 was downregulated by ISO at transcription levels in a SOX2-dependent manner. In addition, ISO attenuated SOX2 expression by specific induction of miR-145, which in turn suppressed 3'UTR activity of SOX2 mRNA without affecting its mRNA stability. Moreover, ectopic expression of exogenous SOX2 rendered D456 cells resistant to induction of cell cycle G0-G1 arrest and anchorage-independent growth inhibition upon ISO treatment, whereas inhibition of miR-145 resulted in D456 cells resistant to ISO inhibition of SOX2 and cyclin D1 expression. In addition,

overexpression of miR-145 mimicked ISO treatment in D456 cells.

Conclusions: ISO induces miR-145 expression, which binds to the SOX2 mRNA 3'UTR region and inhibits SOX2 protein translation. Inhibition of SOX2 leads to cyclin D1 downregulation and PDGS anchorage-independent growth inhibition. The elucidation of the miR-145/SOX2/cyclin D1 axis in PDGS provides a significant insight into understanding the anti-Glioblastoma effect of ISO compound [2].

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Xue Z, Zhao K, Sun Z, Wu C, Yu B, Kong D, Xu B. Isorhapontigenin ameliorates cerebral ischemia/reperfusion injury via modulating Kinase Cε/Nrf2/HO-1 signaling pathway. Brain Behav. 2021 Jun 8:e02143. doi: 10.1002/brb3.2143. Epub ahead of print. PMID: 34102010.

[2]
Xu Z, Zeng X, Xu J, Xu D, Li J, Jin H, Jiang G, Han X, Huang C. Isorhapontigenin suppresses growth of patient-derived glioblastoma spheres through regulating miR-145/SOX2/cyclin D1 axis. Neuro Oncol. 2016 Jun;18(6):830-9. doi: 10.1093/neuonc/nov298. Epub 2015 Dec 17. PMID: 26681767; PMCID: PMC4864260.