Tanshinone

The lipid-soluble diterpene Tanshinone IIA, which was isolated from Salvia miltiorrhiza, has been indicated to reduce cerebral ischemic injury. In this study, we investigated the molecular mechanism of Tanshinone IIA in alleviating reperfusion-induced brain injury.

Methods: Middle cerebral artery occlusion animal models were established, and neurological scores, tetrazolium chloride staining, brain volume quantification, wet and dry brain water content measurement, Nissl staining, enzyme-linked immunosorbent assay, flow cytometry, western blotting, and reverse transcription-quantitative polymerase chain reaction were performed. The viability of cells was measured by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide assays, while cell damage was measured by lactate dehydrogenase release in the in vitro oxygen glucose deprivation model. In addition, enzyme-linked immunosorbent assay, flow cytometry, western blotting, and reverse transcription-quantitative polymerase chain reaction were used to evaluate the therapeutic effect of Tanshinone IIA on ischemia/reperfusion (I/R) induced brain injury, as well as its effects on the inflammatory response and neuronal apoptosis, in vivo and in vitro. Furthermore, this study validated the targeting relationship between miR-124-5p and FoxO1 using a dual luciferase assay. Finally, we examined the role of Tanshinone IIA in brain injury from a molecular perspective by inhibiting miR-124-5p or increasing FoxO1 levels.

Results: After treatment with Tanshinone IIA in middle cerebral artery occlusion-reperfusion (MCAO/R) rats, the volume of cerebral infarction was reduced, the water content of the brain was decreased, the nerve function of the rats was significantly improved, and the cell damage was significantly reduced. In addition, Tanshinone IIA effectively inhibited the I/R-induced inflammatory response and neuronal apoptosis, that is, it inhibited the expression of inflammatory cytokines IL-1β, IL-6, TNF-α, decreased the expression of apoptotic protein Bax and Cleaved-caspase-3, and promoted the expression of antiapoptotic protein Bcl-2. In vitro oxygen-glucose deprivation/reoxygenation (OGD/R) cell model, Tanshinone IIA also inhibited the expression of inflammatory factors in neuronal cells and inhibited the occurrence of neuronal apoptosis. In addition, Tanshinone IIA promoted the expression of miR-124-5p. Transfection of miR-124-5p mimic has the same therapeutic effect as Tanshinone IIA and positive therapeutic effect on OGD cells, while transfection of miR-124-5p inhibitor has the opposite effect. The targeting of miR-124-5p negatively regulates FoxO1 expression. Inhibition of miR-124-5p or overexpression of FoxO1 can weaken the inhibitory effect of Tanshinone IIA on brain injury induced by I/R, while inhibition of miR-124-5p and overexpression of FoxO1 can further weaken the effect of Tanshinone IIA.

Tanshinone IIA alleviates ischemic-reperfusion brain injury by inhibiting neuroinflammation through the miR-124-5p/FoxO1 axis. This finding provides a theoretical basis for mechanistic research on cerebral ischemia-reperfusion injury [1)].

The present study aimed to evaluate the effect of the herbal medicine, tanshinone IIA (Tan IIA), on vestibular schwannoma (VS) cells and assess the functional targets of Tan IIA. HEI-193 cells and Nf2-/-mouse Schwann (SC4) cells were used to investigate the inhibitory effects of Tan IIA on VS. Cell viability was measured using an MTT assay and apoptosis was assessed by flow cytometry. Western blot analysis and reverse transcription quantitative polymerase chain reaction (RT-qPCR) were performed to assess the expression of hypoxia-inducible factor-1α (HIF-1α) and its signaling pathways. In addition, the effect of Tan IIA on HIF-1α transcription was determined using a luciferase reporter assay. Schwannoma cell proliferation was observed to be inhibited as the Tan IIA

concentration increased under normoxic and hypoxic conditions. Furthermore, Tan IIA induced apoptosis in the HEI-193 cells and inhibited the protein expression of HIF-1α in the HEI-193 cells under hypoxia, thus repressing the transcriptional activity of HIF-1α. The present study demonstrated that HIF-1α is expressed in hypoxic VS cells and Tan IIA inhibits VS cells by suppressing the activity of HIF-1α. In conclusion, these results indicate that Tan IIA is a potential chemotherapeutic agent for the treatment of VS [2].

1)
Su W, Lv M, Wang D, He Y, Han H, Zhang Y, Zhang X, Lv S, Yao L. Tanshinone IIA Alleviates Traumatic Brain Injury by Reducing Ischemia–Reperfusion via the miR-124-5p/FoxO1 Axis. Mediators Inflamm. 2024 Mar 21;2024:7459054. doi: 10.1155/2024/7459054. PMID: 38549714; PMCID: PMC10978079.
2)
Kim JY, Song JJ, Kwon BM, Lee JD. Tanshinone IIA exerts antitumor activity against vestibular schwannoma cells by inhibiting the expression of hypoxia-inducible factor-1α. Mol Med Rep. 2015 Jun 15. doi: 10.3892/mmr.2015.3932. [Epub ahead of print] PubMed PMID: 26080622.