Meisoindigo

Meisoindigo, a derivative of Indigo naturalis a second-generation derivative of indirubin, and has general water solubility.

It has been used in China for chronic myeloid leukemia. In vitro cell line studies have shown that this agent might induce apoptosis and myeloid differentiation of acute myeloid leukemia (AML).

It is effective for inhibiting leukocyte chemotactic migration, thus providing a potential therapeutic agent for treating inflammatory diseases [1)].

Ye et al. investigated the hypothesis that meisoindigo was also protective against ischemic stroke, then evaluated its underlying mechanisms. In vivo, adult male C57BL/6 wild-type mice were used to produce a Mouse Model of Middle Cerebral Artery Occlusion On day three after reperfusion, obvious improvement in neurological scores, infarct volume reduction and cerebral edema amelioration were observed in meisoindigo treatment. Moreover, immunofluorescence staining and western blot showed that the expression of NLRP3 inflammasome and its associated proteins in neurons and microglia was inhibited by meisoindigo. The effects of Meisoindigo on NLRP3 inflammasome inactivation and increased the M2 phenotype of microglia/macrophage through shifting from a M1 phenotype, which was possibly mediated by inhibition of TLR4/NF-κB. Furthermore, we verified the inhibitory effect of meisoindigo on TLR4/NF-κB signaling pathway, and found that meisoindigo treatment could significantly suppressed the expression of TLR4/NF-κB pathway-associated proteins in a dose-dependent manner, meanwhile, which resulted in downregulation of HMGB1 and IL-1β. Next, we established an in vitro oxygen glucose deprivation/Reperfusion (OGD/R) model in HT-22 and BV2 cells to simulate ischemic conditions. Cytotoxicity assay showed that meisoindigo substantially improved relative cell vitality and in HT-22 and BV2 cells following OGD/R in vitro. After suffering OGD/R, the TLR4/NF-κB pathway was activated, the expression of NLRP3 inflammasome-associated proteins and M1 microglia/macrophage were increased, but meisoindigo could inhibit above changes in both HT-22 and BV2 cells. Additionally, though lipopolysaccharide stimulated the activation of TLR4 signaling in OGD/R models, meisoindigo co-treatment markedly reversed the upregulation of TLR4 and following activation of NLRP3 inflammasome and polarization of M1 microglia/macrophages mediated by TLR4. Overall, we demonstrate for the first time that meisoindigo post-treatment alleviates brain damage induced by ischemic stroke in vivo and in vitro experiments through blocking activation of the NLRP3 inflammasome and regulating the polarization of microglia/macrophages via inhibition of the TLR4/NF-κB signaling pathway [2)].

Gu et al. explored whether meisoindigo was effective in suppressing proliferation and inducing apoptosis of human glioblastoma multiforme U87 cells and to explore its possible mechanisms.

Morphological changes were observed by light microscopy. Cell counting kit-8 (CCK-8) assay was performed to detect cellular proliferation. Apoptosis was monitored by flow cytometry. Akt, phospho-Akt, PI3K, p65, phospho-p65 and apoptosis-related proteins caspase-3 and caspase-9 were examined by Western blotting assays. Immunofluorescence was used to evaluate level of P65 expression in cells.

Meisoindigo inhibited the proliferation of U87 cells, and the inhibitory effect increased in a dose

dependent manner. Moreover, meisoindigo exposure triggered an increase in the level of caspase-3 and caspase-9, supporting its role in the activation of apoptosis. Furthermore, meisoindigo reduced the expression of PI3K, Akt, phospho-Akt, NF-κB, p65 and phospho-p65 in U87 cells, and displacement of p65 from the nucleus to the cytoplasm.

Meisoindigo inhibits proliferation and induces apoptosis of U87 cells, probably through down-regulating the PI3K/Akt pathway and reducing nuclear translocation of NF-κB p65 [3].

1)
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2)
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3)
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