Shikonin

Shikonin is a major component of zicao (purple gromwell, the dried root of Lithospermum erythrorhizon), a Chinese herbal medicine with various biological activities, including inhibition of human immunodeficiency virus (HIV) type 1 (HIV-1).

Shikonin is a quinone-containing natural product that induces the apoptotic death of some cancer cell lines in culture through increasing intracellular reactive oxygen species (ROS). Quinone-based drugs have shown potential in the clinic, making shikonin an interesting compound to study.

Cell death caused by shikonin in C6 and U87 glioma cells was mainly via necroptosis. Moreover, not only RIP-1 pathway, but also oxidative stress participated in the activation of shikonin induced necroptosis [1)].

Previous study found that shikonin induces apoptosis in neuroblastoma by induction of ROS, but its mechanism of action and scope of activity are unknown. In a study, Yang et al. investigated the mode of oxidative stress of shikonin in human glioma cells. ROS induction by shikonin was of mitochondrial origin, as demonstrated by detection of superoxide with MitoSOX Red. Pre-incubation of shikonin with inhibitors of different complexes of the respiratory chain suggested that shikonin-induced ROS production occurred via complex II. In addition, NADPH oxidase and lipooxygenase are two other main ROS-generated sites in shikonin treatment. ROS production by shikonin resulted in the inhibition of nuclear translocation of Nrf2. Stable overexpression of Nrf2 in glioma cells inhibited ROS generation by shikonin. ROS generation from mitochondrial complex II, NADPH oxidase and lipooxygenase is likely the primary mechanism by which shikonin induces apoptosis in glioma cells. These findings also have relevance to the development of certain ROS producers as anti-cancer agents. These, along with shikonin have potential as novel chemotherapeutic agents on human glioma [2)].

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Huang C, Luo Y, Zhao J, Yang F, Zhao H, Fan W, Ge P. Shikonin kills glioma cells through necroptosis mediated by RIP-1. PLoS One. 2013 Jun 28;8(6):e66326. doi: 10.1371/journal.pone.0066326. Print 2013. PubMed PMID: 23840441; PubMed Central PMCID: PMC3695975.
2)
Yang JT, Li ZL, Wu JY, Lu FJ, Chen CH. An oxidative stress mechanism of shikonin in human glioma cells. PLoS One. 2014 Apr 8;9(4):e94180. doi: 10.1371/journal.pone.0094180. eCollection 2014. PubMed PMID: 24714453; PubMed Central PMCID: PMC3979747.