Matrine

Matrine is a quinolizidine alkaloid derived from the herb Radix Sophorae Flavescentis, and possesses anti-oxidant, anti-inflammatory and anti-tumoral properties.

Glioma cell line U251 cells were treated with matrine to assess viability and proliferation using CCK8 and EdU assays. PI/FITC staining was performed for apoptosis assay. Transfections were performed for circRNA-104075 or Bcl-9 overexpression. Western blot analysis was performed to evaluate changes of protein levels and changes of gene level were detected by qRT-PCR in U251 cells.

Matrine suppressed cell viability while induced apoptosis and autophagy in U251 cells. Matrine also decreased circRNA-104075 expression significantly. Overexpression of circRNA-104075 was found to counteract the inhibitory effects of matrine on cell proliferation and promoting effects on apoptosis and autophagy in U251 cells. Moreover, the suppressed Wnt/β-catenin and PI3K/AKT signaling pathways by matrine were activated by circRNA-104075 overexpression. Furthermore, Bcl-9 expression was also down-regulated by matrine treatment. Bcl-9 overexpression elevated the decreased cell proliferation while suppressed the increased apoptosis and autophagy induced by matrine in U251 cells.

Taken together, the present findings suggested that matrine induced apoptosis and autophagy through down-regulating circ-104075 and Bcl-9 expression via inhibition of PI3K/AKT and Wnt-β-catenin pathways in glioma cells. The present study provides a foundation for further preclinical and clinical evaluations of matrine as a glioma therapy [1)].

In a study, Liu et al., investigated the effects of matrine on early brain injury (EBI) and the related potential mechanisms following SAH in rats. Our results showed that matrine pretreatment partially alleviated SAH-induced EBI, including neurological deficit, severity of SAH grade, brain edema, and blood-brain barrier (BBB) disruption in rats. In addition, SAH procedure induced BBB disruption with concomitant upregulation of MMP-9 expression and downregulation of tight junction proteins expression of BBB, namely, ZO-1 and occludin, which was partially reversed by matrine pretreatment. Matrine also reduced the increased levels of inflammatory cytokines TNF-α and IL-1β after the SAH operation. SAH induced neural cell apoptosis, as demonstrated by high apoptotic index and increased expression of Bax and caspase-3 proteins, as well as the reduced Bcl-2 expression, which were reversed by matrine pretreatment. Furthermore, matrine pretreatment partially suppressed SAH-induced Akt phosphorylation and IκB-α phosphorylation and degradation, and reduced NF-kB P65 protein levels. The expression of Keap1, Nrf2, and HO-1 proteins was distinctly enhanced in the SAH+matrine group, compared with the SAH+vehicle groups. Matrine pretreatment suppressed SAH-induced MMP-9 expression, which could be partially blocked by HO-1 inhibitor Sn-protoporphyrin IX (SnPP IX) but promoted by phosphatidylinositol 3-kinase (PI3K) inhibitor LY294002. Our results suggest that matrine may alleviate EBI after experimental subarachnoid hemorrhage in rats possibly via PI3K/Akt-mediated NF-κB inhibition and Keap1/Nrf2-dependent HO-1 induction [2)].

Unclassified

2: Li L, Chen S, Sun Y, Kong L, Liu G, Guo P. Matrine inhibits the proliferation of pituitary tumor cells by decreasing Foxo3a phosphorylation and promoting Foxo3a nuclear localization. Exp Ther Med. 2019 May;17(5):3775-3780. doi: 10.3892/etm.2019.7365. Epub 2019 Mar 8. PubMed PMID: 30988763; PubMed Central PMCID: PMC6447943.

3: Zhou W, Wang J, Qi Q, Feng Z, Huang B, Chen A, Zhang D, Li W, Zhang Q, Bjerkvig R, Li X, Wang J. Matrine induces senescence of human glioblastoma cells through suppression of the IGF1/PI3K/AKT/p27 signaling pathway. Cancer Med. 2018 Sep;7(9):4729-4743. doi: 10.1002/cam4.1720. Epub 2018 Aug 5. PubMed PMID: 30079478; PubMed Central PMCID: PMC6143938.

4: Wu Z, You Z, Chen P, Chen C, Chen F, Shen J, Xu H. Matrine Exerts Antidepressant-Like Effects on Mice: Role of the Hippocampal PI3K/Akt/mTOR Signaling. Int J Neuropsychopharmacol. 2018 Apr 16. doi: 10.1093/ijnp/pyy028. [Epub ahead of print] PubMed PMID: 29668939; PubMed Central PMCID: PMC6070064.

6: Zhao X, Zhang X, Lv Y, Xu Y, Li M, Pan Q, Chu Y, Liu N, Zhang GX, Zhu L. Matrine downregulates IL-33/ST2 expression in the central nervous system of rats with experimental autoimmune encephalomyelitis. Immunol Lett. 2016 Oct;178:97-104. doi: 10.1016/j.imlet.2016.08.007. Epub 2016 Aug 22. PubMed PMID: 27562326.

7: Zhou K, Ji H, Mao T, Bai Z. Effects of matrine on the proliferation and apoptosis of human medulloblastoma cell line D341. Int J Clin Exp Med. 2014 Apr 15;7(4):911-8. eCollection 2014. PubMed PMID: 24955161; PubMed Central PMCID: PMC4057840.

8: Zheng K, Li C, Shan X, Liu H, Fan W, Wang Z. A study on isolation of chemical constituents from Sophora flavescens Ait. and their anti-glioma effects. Afr J Tradit Complement Altern Med. 2013 Nov 2;11(1):156-60. eCollection 2014. PubMed PMID: 24653570; PubMed Central PMCID: PMC3957258.

9: Xiang J, Jiang Y. Antiepileptic potential of matrine via regulation the levels of gamma-aminobutyric acid and glutamic acid in the brain. Int J Mol Sci. 2013 Dec 5;14(12):23751-61. doi: 10.3390/ijms141223751. PubMed PMID: 24317434; PubMed Central PMCID: PMC3876075.

10: Chen J, Mei Q, Xu YC, Du J, Wei Y, Xu ZM. [Effects of Matrine Injection on T-lymphocyte subsets of patients with malignant tumor after gamma knife radiosurgery]. Zhong Xi Yi Jie He Xue Bao. 2006 Jan;4(1):78-9. Chinese. PubMed PMID: 16409978.

[1)]
Chi G, Xu D, Zhang B, Yang F. Matrine induces apoptosis and autophagy of glioma cell line U251 by regulation of circRNA-104075/BCL-9. Chem Biol Interact. 2019 May 18. pii: S0009-2797(19)30476-4. doi: 10.1016/j.cbi.2019.05.030. [Epub ahead of print] PubMed PMID: 31112718.

[2)]
Liu X, Zhang X, Ma K, Zhang R, Hou P, Sun B, Yuan S, Wang Z, Liu Z. Matrine alleviates early brain injury after experimental subarachnoid hemorrhage in rats: possible involvement of PI3K/Akt-mediated NF-κB inhibition and Keap1/Nrf2-dependent HO-1 inductionn. Cell Mol Biol (Noisy-le-grand). 2016 Sep 30;62(11):38-44. PubMed PMID: 27755950.