Eupatilin

Eupatilin is a major flavonoid from Artemisia plants such as Artemisia princeps and Artemisia argyi which has been reported to possess various beneficial biological effects including anti-inflammation, anti-tumor, anti-cancer, anti-allergy, and anti-oxidation activity.

Eupatilin has a therapeutic effect on inflammation caused by intracerebral hemorrhage. The underlying mechanism may be related to TLR4/MyD88, which brings new hope for clinical patients to improve symptoms and prognosis [1].

Eupatilin inhibits the viability and proliferation of glioma cells, attenuates the migration and invasion, and inhibits tumor growth in vivo, but does not promote apoptosis. Therefore, due to the poor clinical efficacy of drug treatment of glioma and high drug resistance, the emergence of eupatilin brings a new dawn for glioma patients [2]

A study suggest that eupatilin serves neurological protective effects via inhibiting microglial inflammation, providing an experimental basis for the use of eupatilin as a therapeutic target for ICH [3].

Complete blockade of RANK-dependent osteoclastogenesis was accomplished upon stimulation prior to the receptor activator of nuclear factor κB (RANK)-ligand (RANKL) treatment or post-stimulation of bone marrow macrophages (BMCs) in the presence of RANKL with eupatilin. This blockade was accompanied by inhibition of rapid phosphorylation of Akt, GSK3β, ERK, and IκB as well as downregulation of c-Fos and NFATc1 at protein, suggesting that transcriptional suppression is a key mechanism for anti-osteoclastogenesis. Transient reporter assays or gain of function assays confirmed that eupatilin was a potent transcriptional inhibitor in osteoclasts (OC). Surprisingly, when mature osteoclasts were cultured on bone scaffolds in the presence of eupatilin, bone resorption activity was also completely blocked by dismantling the actin rings, suggesting that another major acting site of eupatilin is a cytoskeletal rearrangement. The eupatilin-treated mature osteoclasts revealed a shrunken cytoplasm and accumulation of multi-nuclei, eventually becoming fibroblast-like cells. No apoptosis occurred. Inhibition of phosphorylation of cofilin by eupatilin suggests that actin may play an important role in the morphological change of multinucleated cells (MNCs). Human OC similarly responded to eupatilin. However, eupatilin has no effects on osteoblast differentiation and shows cytotoxicity on osteoblast in the concentration of 50 μM. When eupatilin was administered to LPS-induced osteoporotic mice after the manifestation of osteoporosis, it prevented bone loss. Ovariectomized (OVX) mice remarkably exhibited bone protection effects. Taken together, eupatilin is an effective versatile therapeutic intervention for osteoporosis via; 1) transcriptional suppression of c-Fos and NFATc1 of differentiating OC and 2) inhibition of actin rearrangement of pathogenic MNCs [4]

1)

Fei X, Chen C, Kai S, Fu X, Man W, Ding B, Wang C, Xu R. Eupatilin attenuates the inflammatory response induced by intracerebral hemorrhage through the TLR4/MyD88 pathway. Int Immunopharmacol. 2019 Nov;76:105837. doi: 10.1016/j.intimp.2019.105837. Epub 2019 Aug 30. PMID: 31476693.

2)
Fei X, Wang J, Chen C, Ding B, Fu X, Chen W, Wang C, Xu R. Eupatilin inhibits glioma proliferation, migration, and invasion by arresting cell cycle at G1/S phase and disrupting the cytoskeletal structure. Cancer Manag Res. 2019 May 24;11:4781-4796. doi: 10.2147/CMAR.S207257. PMID: 31213900; PMCID: PMC6539175.
3)
Qiao HB, Li J, Lv LJ, Nie BJ, Lu P, Xue F, Zhang ZM. Eupatilin inhibits microglia activation and attenuates brain injury in intracerebral hemorrhage. Exp Ther Med. 2018 Nov;16(5):4005-4009. doi: 10.3892/etm.2018.6699. Epub 2018 Sep 5. PMID: 30344678; PMCID: PMC6176204.
4)
Kim JY, Lee MS, Baek JM, Park J, Youn BS, Oh J. Massive elimination of multinucleated osteoclasts by eupatilin is due to dual inhibition of transcription and cytoskeletal rearrangement. Bone Rep. 2015 Oct 8;3:83-94. doi: 10.1016/j.bonr.2015.10.003. PMID: 28377971; PMCID: PMC5365243.