Neuroprotective effect of, a flavonoid, sudachitin in mice stroke model

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Abbreviations used: 4-HNE, 4-hydroxynonenal; CARR U, Carratelli units; CC3, cleaved caspase-3; DAB, diaminobenzidine; HPDLC, human periodontal ligament cells; LPS, lipopolysaccharides; MAP-2, microtubule-associated protein-2; MMP, Matrix metalloproteinase; PBS, phosphate-buffered saline; PFA, paraformaldehyde; PGC, peroxisome proliferator-activated receptor-gamma coactivator; ROS, reactive oxygen species; sec, seconds; Sirt1, silent mating type information regulation 2 homolog 1; TNF, tumoral necrosis factor; tMCAO, transient middle cerebral artery occlusion.

ABSTRACT

A flavonoid, sudachitin, has been reported to show some beneficial health effects, including as an anti-inflammatory in LPS-stimulated macrophages, as well as improving glucose and lipid metabolism in mice fed a high-fat diet. In this study, we investigated the neuroprotective effect of sudachitin in the transient middle cerebral artery occlusion (tMCAO) mouse model. After daily pre-treatment of vehicle or sudachitin (5 or 50 mg/kg) for 14 days, mice (n = 76) were subjected to a sham operation or tMCAO for 45 min, and on the following days, they were treated daily with vehicle or sudachitin. The administration of sudachitin significantly reduced ($p < 0.05$) cerebral infarct volume and attenuated apoptosis, 5 days after tMCAO. Neurological impairment improved, the expression of an oxidative stress marker, 4-HNE, decreased, and the Sirt1/PGC-1α pathway was activated 5 days after tMCAO in the sudachitin-treated group. This is the first report to demonstrate the neuroprotective effect of sudachitin in cerebral ischemia/reperfusion injury mice model, probably by activating the Sirt1/PGC-1α axis. Sudachitin may be a promising supplement or therapeutic agent for reducing injury caused by ischemic strokes.

Key words: Sudachitin, transient middle cerebral artery occlusion, ischemia, apoptosis, oxidative stress.