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Protective effect of rice bran oil against neurotoxicity induced by glutamate and ischemia

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글루타메이트와 허혈성 신경독성에 대한 미강유의 보호효과

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Objectives

Ischemic stroke, one of the leading causes of death and long-lasting disability, results from a transient or permanent reduction in cerebral blood flow in a major brain artery. Increased extracellular glutamate levels and subsequent excitotoxicity are thought to be one of the major pathological factors leading to neuronal death in stroke. Rice bran, the major byproduct of the rice milling industry, is the source of a high quality vegetable oil, rice bran oil (RBO). RBO has attracted much medicinal attention due to its strong hypocholesterolemic properties known to be attributable to its balanced fatty acid composition and high levels of antioxidant phytochemicals such as oryzanols, tocopherols and tocotrienols. Therefore, in the present study, we investigated the protective effect of RBO on glutamate- and ischemia- induced neurotoxicity using cultured neurons and middle cerebral artery occlusion (MCAo)/reperfusion rats, respectively.

Materials and Methods

○ Materials

Rice bran oil (RBO), HEX : EtOAc fraction of RBO, glutamate, SD rats

○ Methods

Neuronal cells, cultured from 16-day-old fetuses of SD rats, were treated with glutamate (8 h). Neuronal viability was measured by 3-[4,5-dimethylthiazole-2-yl] -2,5-diphenyl-tetrazolium bromide (MTT) assay. Elevation of the intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) and generation of reactive oxygen species (ROS) induced by glutamate were measured by conforcal microscopy. Cerebral ischemic injury was induced by 2-h MCAo and 24-h reperfusion in SD rats. After MCAo/reperfusion, we measured infarct volume and edema volume of brain.

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Results

RBO (0.1, 1 and 5 μl/ml) inhibited glutamate-induced neuronal cell death.(Fig. 1) Hexane : EtOAc fraction of RBO (HEX : EtOAc = 10 : 1 and 50 : 1 ; 1, 10, 20 μg/ml) inhibited glutamate-induced neuronal cell death. Glutamate induced elevation of $[Ca^{2+}]_i$ and generation of ROS were inhibited by RBO (5 μl/ml) and HEX : EtOAc = 10 : 1, 50 : 1 (20 μg/ml). RBO (3, 5, 10 ml/kg) reduced infarct and edema volume induced by 2-h MCAo and 24-h reperfusion.(Fig. 2) Ischemic rats showed neurological signs, such as circling movement and decreased grip of contralateral forelimb and RBO (10 ml/kg) significantly prevented such behavioral deficits. Rats received RBO (10 ml/kg) showed significantly improved behavior in rotarod test performed 24-h after the reperfusion, compared with rats received corn oil (10 ml/kg) as control. The present study provides an evidence that RBO might be available to protect neurodegeneration in stroke. Furthermore, the protective effect of RBO against ischemia-induced neurotoxicity might be attributable to phytoceramide, as an active principle.

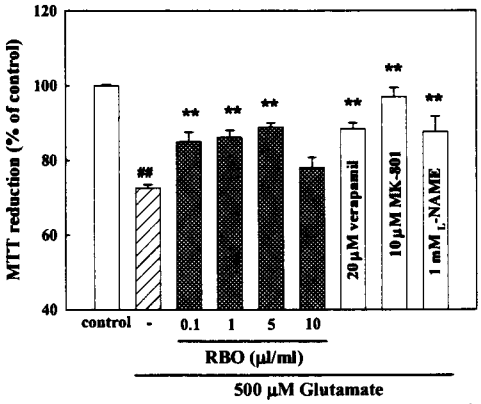

Fig 1. Inhibitory effect of RBO on glutamate-induced neuronal cell death in cultured cortical neurons.

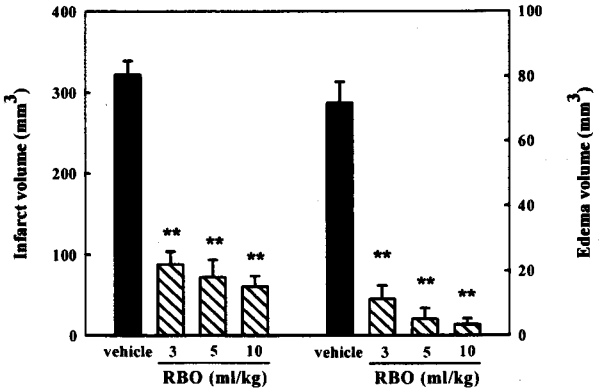

Fig 2. Inhibitory effect of RBO on MCAo-induced infarct formation in rats.