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Anti-ischemic effects of a plants extract complex (SSB)

Joo Youn Kim[1], Hyun Soo Ju[1], KiHwan Bae[2], Kyung-sik Song[3] and Yeon Hee Seong[1*]

[1]College of Veterinary Medicine, Chungbuk National University,
[2]College of Pharmacy, Chungnam National University,
[3]College of Agriculture and Life-Sciences, Kyungpook National University

식물 추출물 복합제 (SSB)의 항허혈효과

충북대학교: 김주연, 주현수, 성연희*
충남대학교: 배기환
경북대학교: 송경식

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. Focal impairment of cerebral blood flow restricts the delivery of metabolic substrates, particularly oxygen, leading to hypoxia. During ischemia/reperfusion condition, there is a heavy production of the free radicals such as superoxide, hydroxyl and hydrogen peroxide (H_2O_2). H_2O_2 and superoxide inhibited the uptake of glutamate and enhanced the release of glutamate, resulting in NMDA receptor overstimulation. Glutamate is one of the principal excitatory neurotransmitters in the brain and its interactions with specific membrane receptors are responsible for many neurological functions. In a variety of pathologic conditions including stroke, excessive activation of glutamate receptors may mediate neuronal injury or death. Such injury appears to be induced by excessive influx of calcium into neurons. In the present study, we investigated anti-ischemic effect of a plants extract complex (SSB) in *in vitro* and *in vivo*.

Materials and Methods

SSB (ethanol extracts of three plants including *Aralia Cordata*) was prepared. Primary cortical neuronal culture was prepared from the forebrains of 16-day-old fetuses from pregnant SD rats. H_2O_2- and glutamate-induced neuronal cell death was measured in cultured cortical neurons. H_2O_2 (100 μM) was treated for 15 min and then neurons were incubated for 12-h in H_2O_2-free medium. Glutamate (500 μM) was treated for 8-h. Hypoxia (2% O_2 and 93% N_2) induced neuronal cell death was measured in cultured rat cerebellar granular cells prepared from 7-day-old neonatals of SD rats. Granular cells were exposed to hypoxia for 24-h and postincubated for

Corresponding author : 성연희 E-mail: vepharm@chungbuk.ac.kr Tel.: 043-261-2968

6-h under normoxia condition. Neuronal cell viability was measured by 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyl-tetrazolium bromide (MTT) assay. Cerebral ischemic injury induced by 2-h middle cerebral artery occlusion (MCAo) and 24-h reperfusion induced focal ischemia was performed in SD rats. SSB (5-25 mg/kg, p.o.) was administered three times at 0.5-h before and 1-h after occlusion, and 1-h after reperfusion. Brain infarct and edema volume and neurological scores were measured.

Results and Discussion

SSB (1-20 μg/ml) showed protective effect against H_2O_2 induced neuronal cell death. Glutamate- and hypoxia-induced neuronal cell death was also significantly inhibited by SSB (1-25 μg/ml). SSB prevented cerebral ischemic injury induced by 2-h MCAo and 24-h reperfusion. Ischemic rats showed neurological signs, such as circling movement and decreased grip of contralateral forelimb. SSB (25 mg/kg) significantly improved the neurological deficits. These results suggest the availability of SSB as a novel therapeutic of neurodegenerative diseases including stroke.

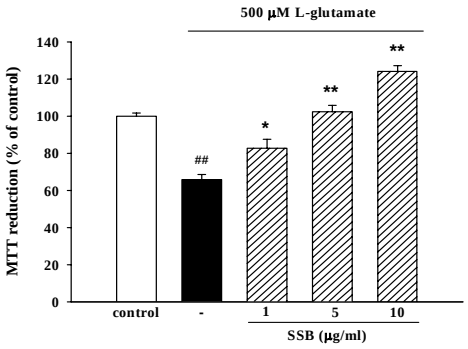

Fig 1. SSB significantly inhibited glutamate induced neuronal cell death measured by MTT assay.

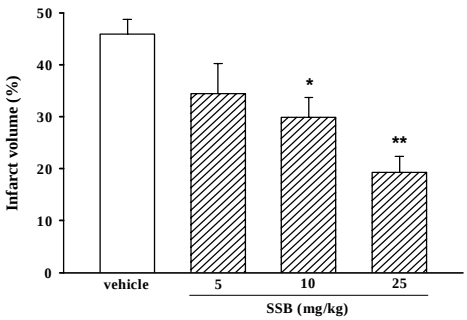

Fig 2. Inhibitory effect of SSB on ischemia-induced infarct formation in rats.