B10

왕머루 포도의 뿌리에서 분리한 heyneanol A의 뇌신경보호효과

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Neuroprotective effect of heyneanol A, derived from the roots of Vitis amurensis Rup

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Objectives

Neurodegenerative diseases are closely associated with oxidative stress. The protective effects of heyneanol A, against brain ischemia and hydrogen peroxide(H_2O_2)-induced oxidative injury to differentiated PC12 cells, were evaluated. The biological activities of plant polyphenols, heyneanol A, were investigated in terms of brain ischemia, glutathione peroxidase (GSH) and reactive oxygen species(ROS) formation. Heyneanol A suppressed GSH depletion as well as ROS formation IN PC12 cells treated by H_2O_2. The neuroprotective potential of heyneanol A was investigated in rats with focal cerebral ischemia induced by middle cerebral artery occlusion and reperfusion. Reperfusion 2 h after MCAO resulted in the increase of infarct sizes of 459.09 ± 21.83 mm^3 in untreated control. In contrast, infarct sizes and edema volumes were significantly inhibited by intravenous treatement of resveratrol(10^{-4}g/kg.) and heyneanol A(10^{-4}g/kg.) in MCAO rats compared with vehicle-treated control rats. These findings suggest that heyneanol A may protect brain ischemia via antioxidant activity and can be used as an anti-ischemic agents.

Materials and Methods

in vitro

1.Protective effects of HeyneanolA against oxidative stress in PC12cells

1. Cell line-PC12 (rat pheochromocytoma line); model system for investigating neuronal cell injury
2. DPPH radical assay
3. Viability assay-H2O2, Heyneanol A (MTT assay)
4. Measurement of intracellular ROS by Flow cytometry
5. GSH content

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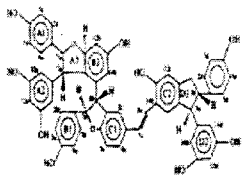
in vivo

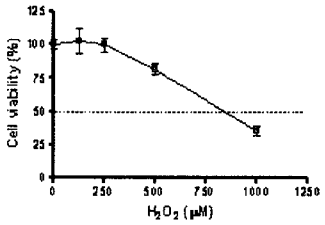
2.Protective effects of HeyneanolA against focal cerebral ischemia from Middle Cerebral Artery Occlusion(MCAO)

1. Middle cerebral artery occlusion induced focal cerebral ischemia
2. Cerebral Infarct volume
3. Cerebral Edema volume
4. Neurological deficits

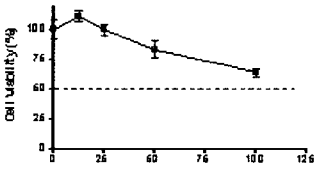
Results



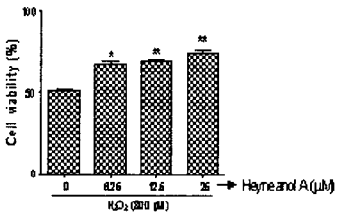
Structure of Heyneanol A



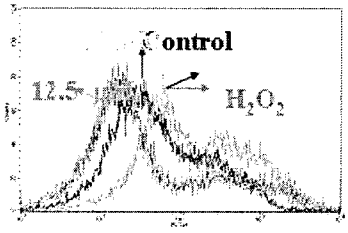
Effects of H_2O_2-induced cytotoxicity on PC12 cells



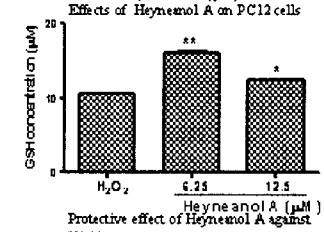
Effects of Heyneanol A on PC12 cells



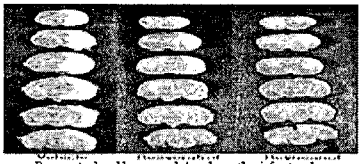
Protective effects of Heyneanol A on PC12 cells exposed to H_2O_2



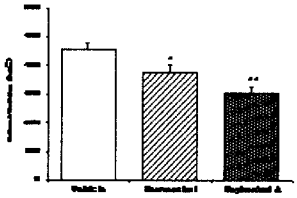
Reduction by Heyneanol A of ROS levels in H_2O_2-treated PC12 cells



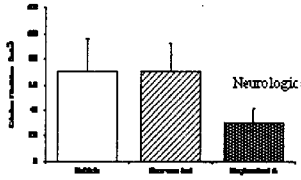
Protective effect of Heyneanol A against H2O2 – induced depletion of GSH



Resveratrol and heyneanol A reduces the infarct volume: TTC-stained coronal sections from representative MCAO-subjected animals



Statistical analysis of infarct volume: infarct volumes were significantly reduced after resveratrol(10-4g/kg, *i.v.*) and heyneanol A(10-4g/kg, *i.v.*) treatment in MCAO rats when compared to the vehicle-treated MCAO rats.



Edema volume after 2h of MCAO and 22h of reperfusion in vehicle, resveratrol(10-4g/kg, *i.v.*) and heyneanol A (10-4g/kg, *i.v.*)treated rats

Neurological score of vehicle, resveratrol and Heyneanol treated MCAO rats

Treatment	N	Neurological score
Vehicle	10	1.60 ± 0.22
Resveratrol (10^{-4}g/kg, i.v.)	10	1.60 ± 0.22
Heyneanol(10^{-4}g/kg, i.v.)	10	1.44 ± 0.22