

damage in the cerebral hemisphere was reduced by 36.3% ($p < 0.01$). Neurological scores were also significantly improved at 24 h after the surgery ($p < 0.01$). These results demonstrate the neuroprotective effect of wogonin in a rat model of permanent occlusion of MCA and provide strong pharmacological basis for the use of *Scutellaria baicalensis* or wogonin in the treatment of stroke.

[PB3-5] [10/17/2002 (Thr) 13:30 – 16:30 / Hall C]

Neuroprotective Effects of Treatment with Aloesin in Rat Model of Permanent Focal Cerebral Ischemia

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Brain injury resulting from cerebral ischemia remains a major public health problem. Aloesin, main component of aloe possesses various biological activities such as wound healing, anti-gastric ulcer, and chemopreventive activity. In this study we investigated whether treatment with aloesin could protect brain injury induced by permanent focal cerebral ischemia in rats. We also compared aloesin with other neuroprotective drugs such as MK801 and ebselen. Permanent focal cerebral ischemia was induced by occlusion of middle cerebral artery for 24 hr without reperfusion in male Sprague-Dawley rat. Neurological deficit scores were measured at 24 hr after onset of ischemia immediately before sacrifice. Coronal slices of the brain were stained 2,3,5-triphenyltetrazolium chloride at 24 hr after onset of ischemia and infarct volumes was measured. Administration of aloesin (10 mg/kg, i.v.) and MK801 (1 mg/kg, i.p.) significantly reduced total infarct volume by 63% and 41%, respectively compared with control group. Ebselen (10 or 30 mg/kg, i.p.) reduced infarct volume but not significantly. Immunohistochemical analysis was done using anti-caspase-3 antibody. DNA fragmentation was confirmed in agarose gel. Activated caspase-3 expression and DNA fragmentation was inhibited by administration of aloesin. The result suggest that aloesin can serve as a lead chemical for the development of neuroprotective agents by providing neuroprotection against permanent focal ischemic brain injury.

[PB3-6] [10/17/2002 (Thr) 13:30 – 16:30 / Hall C]

Erk activation mediates lipopolysaccharide-induced induction of matrix metalloproteinase-9 from rat primary astrocytes

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In central nervous system, matrix metalloproteinases (MMPs) are produced by neuron as well as glia and implicated in physiological events such as neurite outgrowth and myelination etc. In addition, MMPs also contribute to the pathogenesis of several CNS diseases such as multiple sclerosis, Alzheimer's disease and malignant glioma. In spite of their functional importance, little is known about the signal transduction pathways leading to the induction of MMPs in CNS. Here, we investigated whether the activation of Erk(1/2) is involved in the induction of MMP-9 in LPS-stimulated primary astrocytes. The activity, protein and mRNA level of MMP-9 but not those of MMP-2 were increased by LPS treatment, which were assessed by gelatin zymography, immunoblotting and RT-PCR, respectively. LPS treatment induced activation of Erk(1/2) within 30min, which was dose-dependently inhibited by PD98059, a specific inhibitor of the Erk(1/2) kinase (MEK). In this condition, PD98059 blocked the increase in MMP-9 protein and mRNA level as well as gelatin-digesting activity. The treatment of phorbol myristoyl acetate (PMA) activated Erk(1/2) with concomitant increase in MMP-9 production in a dose-dependent manner. The results from the present study suggest that induction of MMP-9 in rat primary astrocytes by LPS is mediated at least in part by the activation of Erk(1/2). The Erk(1/2)-mediated MMP-9 induction may provide insights into the regulation of MMP-9 production in CNS, which may occur in vivo in pathological situations such as CNS inflammation.

[PB3-7] [10/17/2002 (Thr) 13:30 – 16:30 / Hall C]

Cholinergic involvement of spatial memory impairment in μ -opioid receptor knockout mice