題名:Neuroprotective mechanisms of puerarin in middle cerebral artery occlusion-induced brain infarction in rats

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摘要:Puerarin, a major isoflavonoid derived from the Chinese medical herb Radix puerariae (kudzu root), has been reported to be useful in the treatment of various cardiovascular diseases. In the present study, we examined the detailed mechanisms underlying the inhibitory effects of puerarin on inflammatory and apoptotic responses induced by middle cerebral artery occlusion (MCAO) in rats. Treatment of puerarin (25 and 50 mg/kg; intraperitoneally) 10 min before MCAO dose-dependently attenuated focal cerebral ischemia in rats. Administration of puerarin at 50 mg/kg, showed marked reduction in infarct size compared with that of control rats. MCAO-induced focal cerebral ischemia was associated with increases in hypoxia-inducible factor-1alpha (HIF-1alpha), inducible nitric oxide synthase (iNOS), and active caspase-3 protein expressions as well as the mRNA expression of tumor necrosis factor-alpha (TNF-alpha) in ischemic regions. These expressions were markedly inhibited by the treatment of puerarin (50 mg/kg). In addition, puerarin (10-50 microM) concentration-dependently inhibited respiratory bursts in human neutrophils stimulated by formyl-Met-Leu-Phe. On the other hand, puerarin (20-500 microM) did not significantly inhibit the thiobarbituric acid-reactive substance reaction in rat brain homogenates. An electron spin resonance (ESR) method was conducted on the scavenging activity of puerarin on the free radicals formed. Puerarin (200 and 500 microM) did not reduce the ESR signal intensity of hydroxyl radical formation. In

conclusion, we demonstrate that puerarin is a potent neuroprotective agent on MCAO-induced focal cerebral ischemia in vivo. This effect may be mediated, at least in part, by the inhibition of both HIF-1alpha and TNF-alpha activation, followed by the inhibition of inflammatory responses (i.e., iNOS expression), apoptosis formation (active caspase-3), and neutrophil activation, resulting in a reduction in the infarct volume in ischemia-reperfusion brain injury. Thus, puerarin treatment may represent a novel approach to lowering the risk of or improving function in ischemia-reperfusion brain injury-related disorders.