中国中药杂志
China Journal of Chinese Materia Medica

华佗再造浸膏对大鼠局灶性脑缺血/再灌注血脑屏障损伤的保护作用及机制研究

投稿时间： 2012-07-05 责任编辑： 点此下载全文

引用本文：郑咏秋,姚明江,刘建勋,宋文婷,李磊,刘声波,胡燕,锶景希.华佗再造浸膏对大鼠局灶性脑缺血/再灌注血脑屏障损伤的保护作用及机制研究[J].中国中药杂志,2013,38(4):585.

DOI：10.4268/cjcmm20130423

作者中文名	作者英文名	单位中文名	单位英文名	E-Mail
郑咏秋	ZHENG Yong-qiu	中国中医科学院 西苑医院, 北京 100091	Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing 100091, China	
姚明江	YAO Ming-jiang	中国中医科学院 西苑医院, 北京 100091	Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing 100091, China	
刘建勋	LIU Jian-xun	中国中医科学院 西苑医院, 北京 100091	Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing 100091, China	liujx0324@sina.com
宋文婷	SONG Wen-ting	中国中医科学院 西苑医院, 北京 100091	Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing 100091, China	
李磊	LI Lei	中国中医科学院 西苑医院, 北京 100091	Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing 100091, China	
刘声波	LIU Sheng-bo	广州白云山奇星药业有限公司, 广东 广州 510310	Guangzhou Baiyunshan Qixing Pharmaceutical Co., Ltd, Guangzhou 510310, China	
胡燕	HU Yan	广州白云山奇星药业有限公司, 广东 广州 510310	Guangzhou Baiyunshan Qixing Pharmaceutical Co., Ltd, Guangzhou 510310, China	
锶景希	SI Jing-xi	广州白云山奇星药业有限公司, 广东 广州 510310	Guangzhou Baiyunshan Qixing Pharmaceutical Co., Ltd, Guangzhou 510310, China	

基金项目:国家自然科学基金项目(81073087);国家"重大新药创制"科技重大专项(2011ZX09201-201-09)

中文摘要:目的:观察华佗再造浸膏(Huatuo Zaizao extractum,HTZZ)对栓线法阻断大脑中动脉(middle cerebral artery occlusion,MCAO)致大鼠局灶性脑缺血/再灌注(ischemia/reperfusion,I/R)血脑屏障(blood-brain barrier,BBB)损伤的保护作用及其机制。方法:健康成年雄性Sprague-Dawley大鼠60只,随机分为假手术组,MCAO模型组,达纳康组(20 mg·kg^{-1}),HTZZ高、中、低剂量组(5,2.5,1.25 g·kg^{-1}),每组10只,十二指肠单次给药。采用栓线法阻断大脑中动脉,建立大鼠局灶性I/R模型。缺血90 min,再灌注24 h后,HE染色观察缺血侧病理损伤,透射电镜观察血脑屏障结构,蛋白免疫印记法检测G蛋白偶联受体激酶2(G protein-coupled receptor kinases 2,GRK2),基质金属蛋白酶-2(matrix metalloproteinases,MMP-2)和MMP-9表达。结果:90 min MCAO/24 h再灌注半暗带皮层脑微血管呈现水肿、线粒体损伤、空泡化、膜损伤和微绒毛减少等。伴随这一变化,损伤侧皮层半暗带脑组织GRK2亚细胞分布从胞浆向胞膜转移,MMP-2和MMP-9表达升高。HTZZ可有效恢复脑缺血再灌注造成的脑微血管内皮水肿和血脑屏障超微结构损伤,减少功能性(膜偶联)GRK2表达,并抑制MMP-2和MMP-9表达。结论:细胞膜偶联GRK2可能是华佗再造丸的有效作用靶点。

中文关键词:华佗再造浸膏 大脑中动脉栓塞 缺血/再灌注 血脑屏障 G蛋白偶联受体激酶

Effect and mechanism of Huatuo Zaizao extractum on focal cerebral ischemia/reperfusion-induced blood-brain barrier inury in rats

Abstract:Objective: To observe the effect and mechanism of Huatuo Zaizao extractum (HTZZ) on focal ischemia/reperfusion (I/R) blood-brain barrier injury induced by middle cerebral artery occlusion. **Method:** Sixty healthy male adult Sprague-Dawley rats was randomly

divided into the sham operation group, the MCAO model group, the Tanakan (20 mg • kg^{-1}) group, and high, middle and low-dose HTZZ groups (5, 2.5, 1.25 g • kg^{-1}), with 10 in each group and single-dose duodenal administration. Middle cerebral artery occlusion was adopted to establish the rat focal I/R model. After ischemia for 90 min and reperfusion for 24 h, the pathological injury at the ischemia side was observed by HE staining. The blood-brain barrier structure was observed under transmission electron microscope. Expressions of G protein-coupled receptor kinases 2 (GRK2), matrix metalloproteinases 2 (MMP-2) and MMP-9 were detected by western blotting technique. **Result:** After 90 min MCAO/24 h reperfusion, penumbra cerebral cortical micro-vessels showed edema, mitochondrial injury, vacuolation, membrane injury and reduction. Along with the changes, sub-cells of G protein-coupled receptor kinase 2 (GRK2) in cortical penumbra brain tissues transferred from cytoplasm to membrane, with increase in expressions of MMP-2 and MMP-9. HTZZ could effectively recover cerebral micro-vascular endothelial edema and blood-brain barrier ultra-structure injury induced by I/R, reduce expression of functional (membrane coupling) GRK2, and inhibit expressions of MMP-2 and MMP-9. **Conclusion:** Cell membrane coupling GRK2 may be the effective target of Huatuo Zaizao extractum.

keywords: Huatuo Zaizao extractum middle cerebral artery occlusion ischemia/reperfusion blood-brain barrier G protein-coupled receptor kinases