

Neuroprotective Effect of *Crocus sativus* against Cerebral Ischemia in Rats

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Abstract : Disorders of the cerebral circulation are the leading cause of numerous neurological and psychiatric illnesses. The transient middle cerebral artery occlusion model (MCAO) is considered to be a reliable and reproducible rodent model of cerebral ischemia. The purpose of the current study was to examine the neuroprotective effects of *Crocus sativus* (saffron) in a rat model of left middle cerebral artery MCAO. Male Wistar rats were anesthetized and subjected to 1 h of MCAO followed by 48 h reperfusion or sham surgery. One group of the ischemia operated animals was kept as left brain ischemia/reperfusion (I/R). Another 2 operated groups received saffron extract (100 or 200 mg/kg, i.p) four times (60 min before the surgery, during the surgery, and on days 1 and 2 after the occlusion). During the experiment, behavioral tests were performed. After 72 h the animals were euthanized and their left brain hemispheres were used in the biochemical, histopathological, and immunohistochemical studies. Saffron administration revealed an improvement in I/R-induced alteration of locomotor balance and coordination ability of rats. Moreover, saffron decreased the brain content of malondialdehyde, nitric oxide, brain natriuretic peptide and vascular endothelial growth factor with significant increase of reduced glutathione. Immunohistochemical evaluation of caspase-3 and Bax protein expression revealed reduction in I/R-enhanced apoptosis in saffron treated rats. In conclusion, saffron treatment decreases ischemic brain injury in association with inhibition of apoptotic and oxidative cell death in a dose dependent manner.

Keywords : caspase-3, cerebral ischemia, *Crocus sativus*, rats, vascular endothelial growth factor

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