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**Crocin as an active ingredient of saffron attenuates cognitive deficits due to intracerebroventricular injection of colchicine in the rat**

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Background and Objective: Cognitive dysfunction is a typical phenotype of Alzheimer's disease (AD). Crocin has shown beneficial effect in different models of cognitive decline. In this study, we evaluated whether crocin could prevent cognitive dysfunction due to intracerebroventricular injection of colchicine in the rat.

Materials and Methods: Male rats (n = 32) were assigned to four experimental groups as follows: Sham, lesion (receiving intracerebroventricular colchicine bilaterally at a dose of 15 microg), and two lesion groups receiving crocin p.o. at doses of 10 or 50 mg/kg in addition to colchicine. Finally, passive avoidance and Y-maze tests were used to assess cognition.

Results: Our data demonstrated that intracerebroventricular colchicine could significantly lower alternation in Y-maze and step-through latency in passive avoidance and administration of crocin to lesion group at a dose of 50 mg/kg could significantly improves performance of animals in these tasks.

Conclusion: Crocin at a dose of 50 mg/kg could effectively ameliorate learning and memory decline due to intracerebroventricular injection of colchicine in the rat.

Keywords: Colchicine, Cognitive decline, Crocin, Saffron

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**Orexin is involved in naloxone induced hyperactivity of locus coeruleus in morphine dependent rats**

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Background and Objective: Repetitive administration of opioid agonists is associated with the induction of dependency to the effects of these substances and thus limits their application. The locus coeruleus (LC) is a key brain structure implicated in opiate dependency and tolerance. Orexin is involved in morphine tolerance and dependence and its type 1 receptor (OXR1) has been detected in LC nucleus. We studied the effect of OXR1 blockade on naloxone induced hyperactivity of LC neurons in morphine dependent rats.

Method: Male Wistar rats weighing 250-300 g were used in this study. To incite dependency, morphine was injected (10 mg/kg, i.p.) twice a day for 10 days. The LC neural activity was investigated using in vivo extracellular single unit recording. A selective OXR1 antagonist (SB-334867) was microinjected into the right cerebral ventricle (10 μg/10 μl. i.c.v.) while recording, immediately before naloxone injection. In the molecular level we used RT-PCR in order to measure the expression of orexin 1 receptor in LC neurons.

Results: Morphine injection during 10 days led to the induction of morphine dependency in LC neurons which was observed as a significant increase in responsiveness of LC neurons to naloxone injection. Administration of SB-334867 before naloxone injection attenuated naloxone induced hyperactivity of LC neurons. Furthermore, chronic administration of morphine caused an increase in OXR1 expression in LC.

Conclusion: The results indicate that orexin receptors are involved in naloxone induced hyperactivity of LC neurons and morphine withdrawal signs

Keywords: Morphine, Locus coeruleus nucleus, Orexin, Single unit recording, RT-P