Summary of the DVM thesis No:28695 , Faculty of Veterinary Medicine, Urmia University.
The academic year: 2025

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Title: Effects of crocetin on pathophysiological changes (behavior and hippocampal histopathology) induced by long-term morphine administration in rats

Abstract:
Morphine is the active ingredient of crude opium and has analgesic and pharmacological properties. In addition to its analgesic effect, morphine is involved in various physiological and pathophysiological processes, including stress, learning and memory, food and water intake, motor functions, and general activity. However, morphine can also cause severe side effects in different tissues, particularly in the nervous system. Crocetin, a biologically active constituent of saffron, has been reported to possess neuroprotective, sleep-enhancing, and anti-neuropathic pain properties. This study investigated the pathophysiological changes in the hippocampus induced by long-term morphine administration and the potential protective effects of crocetin. Twenty-four male rats were randomly divided into four groups (six rats per group): control group, morphine group (20 mg/kg), crocetin (2.5 mg/kg) + morphine (20 mg/kg) group, and crocetin (10 mg/kg) + morphine (20 mg/kg) group. Morphine was administered intraperitoneally for 28 days, while crocetin was administered orally by gavage. Memory and learning were assessed using the Morris water maze test, and hippocampal histopathological changes were examined using light microscopy. In the morphine group, spatial memory and learning impairments were observed, along with histopathological alterations such as edema, vacuolation, and neuronal shrinkage. The results demonstrated that crocetin at a higher dose (10 mg/kg) ameliorated the histopathological changes and behavioral deficits induced by morphine.

Keywords: crocetin, hippocampus, learning and memory, morphine, rat