

**Abstract:**

Muscle pain is a common acute and chronic pain, especially in the sports community and the elderly population. The treatment of muscle pain with synthetic drugs has not brought much success, which has led to the use of herbal drugs and their active ingredients. Curcumin is the active ingredient of turmeric, which is used to treat various pains, including neuropathic pain and joint pain. This study was carried out in order to determine the mechanisms of muscle pain-relieving effect of curcumin in male Wistar rats in the weight range of 220 - 250 grams. Animals were divided into two main groups with peripheral and central administration, and each of the main groups was divided into several subgroups for peripheral and central administration of drugs. Muscle pain was caused by intramuscular injection of 2.5% formalin into the right gastrocnemius muscle. Curcumin was administered orally by gavage. Local effects with intramuscular injection of antagonists of nitric oxide system (L-NAME) and cyclooxygenase system (diclofenac) and central effects with intracerebroventricular injection of antagonists of opioid system (naloxone) and cannabinoid system (AM-251) alone and after curcumin were investigated. The obtained results showed the muscle pain-relieving effects of curcumin (25 and 100 mg/kg body weight). Intramuscular injection of diclofenac (10 mg/kg body weight) alone had no effect, while 40 mg/kg body weight of diclofenac suppressed the pain response in the second stage. Intramuscular injection of diclofenac at a dose of 40 mg/kg body weight enhanced the pain-reducing effect of curcumin (100 mg/kg body weight). Intramuscular injection of L-NAME at 40 mg/kg body weight and not at 10 mg/kg body weight reduced the second-phase pain response and did not enhance the inhibitory effect of curcumin. Diclofenac and L-NAME injections at the same dose of 40 mg/kg body weight in the contr-lateral gastrocnemius muscle did not affect muscle pain responses. Intracerebroventricular injection of naloxone at the doses of 0.5 and 2 µg alone did not affect the muscle pain response, and at a dose of 2 µg, it prevented the pain-suppressing effect of curcumin. Intracerebroventricular injection of AM-251 at a dose of 0.5 µg reduced the muscle pain response, while it did not produce an effect at a dose of 2 µg. Also, AM-251 at a dose of 0.5 µg enhanced the analgesic effect of curcumin, while it prevented it at a dose of 2 µg. The treatments mentioned above did not affect the locomotor behavior. According to the obtained results, it can be stated that curcumin produced a reducing effect on the neurogenic and inflammatory phases of muscle pain caused by formalin. Both cyclooxygenase and nitric oxide systems were involved in the inflammatory phase of muscle pain. In reducing inflammatory pain, curcumin employed the local mechanism of the cyclooxygenase enzyme pathway and in reducing neurogenic and inflammatory pain, the central mechanisms of the opioid and cannabinoid systems might be used.

**Keywords:** Curcumin, Diclofenac, L-NAME, Naloxone, AM-251, muscle pain, rat