

## Effects of *Stachys byzantina* C. koch aerial parts aqueous extract on morphine dependence and tolerance in mice

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**Background and Aims:** Due to interaction of Lamiaceae plants with opioid system, we decided to evaluate the effect of another plant of this family, *Stachys byzantina* C. Koch., on withdrawal syndrome and tolerance to antinociceptive action of morphine.

**Methods:** Dependence was induced using subcutaneous (S.C) injection of morphine daily for 3 days. On day 4, morphine was injected 0.5 h after the intraperitoneal (i.p) injection of extract or clonidine (0.3 mg/kg, as positive control). Naloxone was injected (5 mg/kg, S.C) 2h after the final dose of morphine. The number of episodes of jumping during 30 minutes after injection of naloxone was considered as the intensity of the withdrawal syndrome. Tolerance to morphine was induced by twice-daily injection of morphine (20 mg/kg, S.C.) for 4 days. The antinociceptive response to morphine (10mg/kg, S.C) was determined on day 1 and 6 using the tail flick test. The effect of different doses of aqueous extract of *S.byzantina* (0.04-0.4 g/kg), twice-daily, was determined on tolerance to the antinociceptive action of morphine. The aqueous extract was not injected on day 6. The locomotor activity of the aqueous extract was evaluated using the openfield activity test in mice.

**Results:** The aqueous extract decreased the jumping episode significantly. In addition, the aqueous extract of *S. byzantina* attenuated the development to tolerance to the antinociceptive action of morphine in mice. None of doses reduced the locomotion activity in mice.

**Conclusions:** We can conclude that the aqueous extract of *S. byzantina* reduced morphine withdrawal syndrome and tolerance.

**Keywords:** *Stachys byzantina*; Morphine dependence; Withdrawal syndrome