

# Abstract

**Background:** Cannabinoids are the most widely used illicit substances. Cannabis strains with high THC content, which are currently the most common, are linked to higher risk of addiction development. Studies proved the role of ghrelin and its receptor GHS-R1A in the brain reward system, which is crucial for reinforcing effects of palatable food and drugs of abuse. Because the role of ghrelin in rewarding effects of cannabinoids wasn't widely studied, we tested this relationship using the conditioned place preference (CPP) method.

**Aim:** Using the rat model, to find out if: **(A)** acute premedication with GHS-R1A antagonist influences the manifestation of THC-induced place preference; **(B)** co-administration of the GHS-R1A antagonist together with THC during conditioning suppresses the development of CPP.

**Methods:** Male rats (Wistar) were separated into three groups for both experimental arrangements (JMV2959 dosage of 0, 1 or 3 mg/kg). First day we determined natural preference of the rats for one of the compartments (20 min). 2-9th day the conditioning took place, where THC (0,3 mg/kg i.p.) in the less preferred compartment and saline in the preferred compartment were administered. 10th day we again observed preference of the rats for one of the compartments. In arrangement **(A)** acute application of JMV2959 on the 10th day, prior to the test session, was performed. In arrangement **(B)** JMV2959 was co-administered with THC during conditioning.

**Results:** **(A)** acute JMV2959 administration significantly and dose-dependently reduced the THC-induced CPP manifestation/THC-seeking behavior. **(B)** Repeated administration of JMV2959 together with THC during conditioning significantly attenuated the THC rewarding/reinforcing effects, which consequently reduced the THC - place association, thus the CPP development.

**Conclusion:** The experiment demonstrated an important role of ghrelin/GHS-R1A in reinforcing/rewarding effects of THC. Our results support further research of ghrelin antagonism as a potential new strategy in cannabis addiction treatment.

**Key words:** tetrahydrocannabinol - addiction - ghrelin antagonism - conditioned place preference