

# **Tolerance to hypothermic and antinociceptive effects of $\Delta^9$ -tetrahydrocannabinol (THC) vapor inhalation in rats.**

## **Abstract**

### **RATIONALE:**

A reduced effect of a given dose of  $\Delta^9$ -tetrahydrocannabinol (THC) emerges with repeated exposure to the drug. This tolerance can vary depending on THC dose, exposure chronicity and the behavioral or physiological measure of interest. A novel THC inhalation system based on e-cigarette technology has been recently shown to produce the hypothermic and antinociceptive effects of THC in rats.

### **OBJECTIVE:**

To determine if tolerance to these effects can be produced with repeated vapor inhalation.

### **METHODS:**

Groups of male and female Wistar rats were exposed to 30 min of inhalation of the propylene glycol (PG) vehicle or THC (200 mg/mL in PG) two or three times per day for four days. Rectal temperature changes and nociception were assessed after the first exposure on the first and fourth days of repeated inhalation.

### **RESULTS:**

Female, but not male, rats developed tolerance to the hypothermic and antinociceptive effects of THC after four days of twice-daily THC vapor inhalation. Thrice daily inhalation for four days resulted in tolerance in both male and female rats. The plasma THC levels reached after a 30 min inhalation session did not differ between the male and female rats.

### **CONCLUSIONS:**

Repeated daily THC inhalation induces tolerance in female and male rats, providing further validation of the vapor inhalation method for preclinical studies.