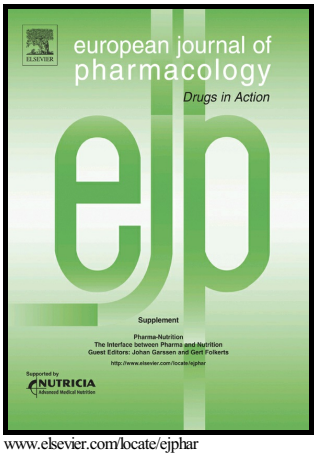

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PII: S0014-2999(18)30310-8
DOI: https://doi.org/10.1016/j.ejphar.2018.05.041
Reference: EJP71823

To appear in: *European Journal of Pharmacology*

Received date: 9 January 2018
Revised date: 24 May 2018
Accepted date: 25 May 2018

Cite this article as: Peter F Weed, Lisa R Gerak and Charles P France, Ventilatory-depressant effects of opioids alone and in combination with cannabinoids in rhesus monkeys, *European Journal of Pharmacology,* https://doi.org/10.1016/j.ejphar.2018.05.041

Ventilatory-depressant effects of opioids alone and in combination with cannabinoids in rhesus monkeys

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Abstract

Pain is a serious health problem that is commonly treated with opioids, although the doses of opioids needed to treat pain are often similar to those that decrease respiration. Combining opioids with drugs that relieve pain through non-opioid mechanisms can decrease the doses of opioids needed for analgesia, resulting in an improved therapeutic window, but only if the doses of opioids that decrease respiration are not similarly decreased. Using small doses of opioids to treat pain has the potential to reduce the number of overdoses and deaths. This study investigated whether the cannabinoid receptor agonists Δ^9-tetrahydrocannabinol (Δ^9-THC) and CP 55,940 modify the ventilatory-depressant effects of morphine and fentanyl in three monkeys. Ventilatory parameters, including minute volume (V_E), were monitored with a head plethysmograph. When given alone, morphine (0.032 – 10 mg/kg) and fentanyl (0.00032 – 0.1 mg/kg) dose dependently decreased V_E. Doses of Δ^9-THC (1 mg/kg) and CP 55,940 (0.01 mg/kg) that enhance the potency of opioids to produce antinociception, alone modestly decreased ventilation but did not significantly change morphine or fentanyl dose-effect curves. A larger dose of CP 55,940 (0.032 mg/kg) shifted the fentanyl dose-effect curve downward in two monkeys, without significantly changing the morphine dose-effect curve. In summary, cannabinoid receptor agonists, which