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"Effects of NEPE14 on Condition Behavior and Nociception"

Introduction: As the highly addictive and dangerous effects of opioids are becoming more widely known, cannabinoids have been discussed as a potential replacement for opioids in the mitigation of pain. Our research has examined the effects of a non-euphoric phytocannabinoid elixir, NEPE14, on thermal nociception and conditioned behavior by giving Sprague Dawley rats NEPE14 sublingually (s.l.) and intraperitoneally (i.p.). A model of Complete Freud's Adjuvant (CFA)-induced hyperalgesia was also used to assess the effects of NEPE14 on chronic inflammation-induced mechanical and thermal pain in another group of subjects.

Methods: Nine subjects were first trained to respond under a fixed-ratio 30 (FR-30) schedule of food presentation. During these behavioral sessions, overall response rate, run rate, and pre-ratio pause duration were recorded. Immediately after these behavioral sessions, warm-water tail-withdrawal latency (in seconds) was assessed using 40 or 50 °C water. To assess the effects of NEPE14, subjects were injected with it 30 minutes prior to the behavioral testing sessions once or twice per week until complete dose-effect curves were established. After CFA injection in the second group of rats, hindpaw withdrawal was tested in rats given NEPE14 and compared to vehicle-treated rats. Mechanical and thermal hypersensitivity was measured by Von Frey filament mechanical sensitivity testing and cold plate thermal sensitivity testing, respectively.

Results: Acute administration of NEPE14 (3.7-20.7 ml/kg i.p., or 0.1-1 ml s.l.) did not significantly affect either response rate or tail-withdrawal latency. However, there was a small, but significant increase in run rate at the 3.7 and 11.8 ml/kg volume. In the CFA rats tested for mechanical hyperalgesia, there was a main effect of both NEPE14 volume ($p= 0.0433$) and a main effect of CFA ($p<0.0001$). When tested for thermal hyperalgesia there was a main effect of dose ($p=0.0261$) and a main effect of CFA ($p=0.0181$). These results show that NEPE14 alleviated both mechanical and thermal hyperalgesia in CFA-treated female rats.

Conclusion: NEPE14 i.p. or s.l. did not significantly affect either conditioned behavior or tail-withdrawal latency in the absence of chronic inflammatory pain. However, both i.p. and s.l. NEPE14 decreased chronic CFA-induced mechanical and thermal hyperalgesia, suggesting that it may be effective for treating chronic inflammatory pain.