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**A COMPARISON OF THE EFFECT OF MORPHINE AND FENTANYL DERIVATIVES ON THE ANTINOCCEPTION AND BODY TEMPERATURE IN RATS**

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**Introduction:** In addition to producing antinociception, opioids exert profound effects on body temperature.

**Aim:** This study aimed at comparing antinociceptive and hyperthermic responses between two groups of  $\mu$ -opioid receptor agonists: fentanyl (4-anilinopiperidine-type) and morphine (phenanthrene-type) derivatives in rats.

**Methods:** Analgesic activity was assessed by tail-immersion test in male Wistar rats (200-250 g). The distal 5 cm of the tail was immersed in a warm water bath ( $55 \pm 0.5^\circ\text{C}$ ) and the time for tail-withdrawal was measured as a response latency. The body temperature was measured by insertion of a thermometer probe 5 cm into the colon of unrestrained rats.

**Results:** Fentanyl (F), ( $\pm$ )cis-3-methyl fentanyl (CM), ( $\pm$ )cis-3-carbomethoxy fentanyl (C), ( $\pm$ )trans-3-carbomethoxy fentanyl (T) and ( $\pm$ )cis-3 butyl fentanyl (B) produced dose-dependent increase in antinociception and hyperthermia. The relative order of analgesic potency was: CM(11.27)>F(1)>C(0.35)<sup>3</sup>T(0.11)<sup>3</sup>B (0.056). Similar to this, the relative order of hyperthermic potency was: CM(8.43)>F(1)>C(0.46)<sup>3</sup>T(0.11)<sup>3</sup>B(0.076). Morphine (M), oxycodone (O), thebacon (T) and 6,14-Ethenomorphinan-7-methanol, 4,5-epoxy-6-fluoro-3-hydroxy-a,a,17-trimethyl-, (5a,7a) (E) also produced dose-dependent increase in antinociception and hyperthermia. Among morphine derivatives the relative order of analgesic potency was: E(56)>O(5)<sup>3</sup>T(2.6)>M(1), and similar to this, the relative order of hyperthermic potency was: E(37)>O(3)<sup>3</sup>T(2.3)>M(1).

**Conclusion:** Morphine (phenanthrene-type) and fentanyl (4-anilinopiperidine-type) derivatives produced hyperthermia in rats at doses about 2 times lower, and 6 to 11 times higher, than their median antinociceptive doses, respectively. This study is first to identify difference between these two classes of opioid drugs in their potencies in producing hyperthermia.