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**SYNERGISTIC ANTINOCICEPTIVE EFFECT OF IBUPROFEN AND HYDROCODONE IN AN ACUTE PAIN MODEL IN RATS**

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**Introduction:** Ibuprofen, a nonsteroidal anti-inflammatory drug, attenuates pain partly by inhibition of the production of prostenoids by cyclooxygenase (COX). Hydrocodone is a mu-opioid receptor agonist that inhibits nociception by spinal pre and postsynaptic mu-opioid receptor activation. Both drugs are used for pain states generated by peripheral injury/inflammation. This study is to investigate whether ibuprofen and/or hydrocodone produce antinociception in an acute pain model in rats, and whether the combination of these two agents is super- or sub-additive.

**Methods:** The Ad/C foot withdrawal test was used. Latencies were measured to foot withdrawal of rat hindpaws elicited by either high (6.5 °C/s) or low (0.9 °C/s) average heating rate before and after i.m. application of ibuprofen and/or hydrocodone or vehicle.

**Results:** Intra-muscular application of either ibuprofen (25, 50, 75, 100, 200mg/kg) or hydrocodone (0.5, 1, 2.5, 5mg/kg) produced dose-dependent antinociception with an ED50 of 85.0mg/kg SEM (standard deviation) 2.3 and an ED50 = 1.3mg/kg SEM 0.15 for C fiber mediated responses. I.m. vehicle had no effect in the test. The combined i.m. administration of ibuprofen (25.4 MPE % (a percent of the maximum possible effect)) and hydrocodone (5.6 MPE %) produced a synergistic (51.9MPE%) antinociceptive effect.

**Conclusions:** These findings suggest that prostanoid production via COX pathway may play a role in C fiber mediated acute pain, and that the synergistic combination of ibuprofen and hydrocodone may be clinically useful.

**References**

1. Palangio M. et al: Dose-response effect of combination hydrocodone with ibuprofen in patients with moderate to severe postoperative pain. *Clinical Therapeutics* 2000, Vol 22, Issue 8: 990-1002. 2. Palangio M. et al: Combination hydrocodone and ibuprofen versus combination codeine and acetaminophen for the treatment of chronic pain. *Clinical Therapeutics* 2000, Vol 22, Issue 8: 990-1002. 3. Sunshine A. et al: Analgesic efficacy of a hydrocodone with ibuprofen combination compared with ibuprofen alone for the treatment of acute postoperative pain. *J Clin Pharmacol* 1997 Oct; 37(10):908-915.