Tolerance to analgesia dependence liability by topical application of dihydroetorphine to hairless rats

Satoshi Ohmori (大森悟史), Liang Fang (方 亮), Masami Kawase (河瀨雅美), Setsuo Saito (齋藤節生), Yasunori Morimoto (森本雍憲)*

Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Josai University, 1-1 Keyakidai, Sakado, Saitama 350-0295, Japan

The tolerance analgesia and dependence liability of dihydroetorphine following topical application were investigated in hairless rats with and without formalin-induced inflammation. The analgesic effect of dihydroetorphine (s.c.) was 4600-to 7200-fold more potent than that of morphine. In non-inflamed rats, the analgesic effect of 24-h topical application of dihydroetorphine tape (35 µg) and 4-day repeated tape applications (20 µg/5h/day) decreased with time after the start of application, even though the plasma dihydroetorphine concentrations did not decrease. Informalin-inflamed rats, however, the tolerance to analgesia diminished. Naloxone-precipitated weight loss was observed after 24-h infusion of dihydroetorphine but not after the tape application in non-inflamed rats. A significant rewarding effect was found in the non-inflamed rats conditioned by s.c. injection and tape application but not in the formalin-inflamed rats. These results indicate that topical application of dihydroetorphine has a tolerance and dependence liability when there is no pain, and therefore, it should be used only for pain relief.