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Category:VSTi pluginsReversal of opiate-induced respiratory depression in mice by novel pyridoindole analogues. Opiate-induced respiratory depression has been used as an animal model for analgesic drugs. In this study, effects of novel pyridoindole derivatives on the respiratory depression were examined. Respiratory depression was induced by s.c. injection of beta-endorphin at 0.1, 0.3 or 1.0 mg/kg in mice. This dose of beta-endorphin elicited no mortality, but significantly decreased the respiratory rate and tidal volume in a dose-dependent manner. Pentylenetetrazol (PTZ) (100 mg/kg, i.p.) increased the respiratory rate and tidal volume in mice and was able to antagonize the respiratory depression induced by beta-endorphin at all doses. In contrast, the respiratory depression induced by beta-endorphin was not antagonized by pentobarbital (50 mg/kg, i.p.). Four pyridoindole derivatives, MK-0677, N,N-dimethyl-5,7-dihydroxy-3-[2-[4-(2- pyridyl)piperazinyl]ethyl]-1,4-dihydro-2H-pyrido[1,2-a]pyridin-1-one dihydrochloride, N,N-dimethyl-5,7-dihydroxy-3-[2-[3-[4-(3- pyridyl)piperazinyl]propyl]-1,4-dihydro-2H-pyrido[1,2-a]pyridin-1-one dihydrochloride and N,N-dimethyl-5,7-dihydroxy-3-[2-[2-(3-pyridyl)piperazinyl]ethyl]-1,4-dihydro-2H-pyrido[1,2-a]pyridin-1-one dihydrochloride were found to be more potent than pentobarbital in reversing the respiratory depression induced by beta-endorphin. MK-0677 (1-10 mg/kg, s.c.), N,N-dimethyl-5,7-dihydroxy-3-[2-[4-(2- p 2d92ce491b