

Synergy between the antinociceptive effects of morphine and NSAIDs

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The intraperitoneal administration of morphine, diclofenac, ketoprofen, meloxicam, metamizol, paracetamol and piroxicam induced dose-dependent antinociception in mice tested with the acetic acid writhing test. The isobolographic analysis of the simultaneous intraperitoneal administration of fractions of the ED₅₀'s of morphine with each nonsteroidal anti-inflammatory drug (NSAID) demonstrated the existence of a supra-additive interaction (synergy). The selective antagonist of μ -opioid receptors naltrexone partially reversed the supra-additive interactions to additive interactions; however, the combinations of morphine/metamizol and morphine/paracetamol were completely antagonized, resulting in subadditive interactions. The selective antagonist of μ -opioid receptors naltrindole failed to significantly attenuate the combinations of morphine with ketoprofen, meloxicam and piroxicam, but decreased the activity of the combinations of morphine with diclofenac, metamizol and paracetamol, trans