

## Synergism between NSAIDs in the orofacial formalin test in mice

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Opioids and non-steroidal anti-inflammatory drugs (NSAIDs) are used to relieve acute and chronic pain. The purpose of this study was to determine the degree of interaction between dexketoprofen and NSAID examples of COXs inhibitors using the isobolographic analysis in the formalin orofacial test in mice. The drugs, i.p., induced a dose-dependent antinociception with different potencies in both test phases. Combinations of dexketoprofen with naproxen, nimesulide, ibuprofen or paracetamol on the basis of the fixed ratio (1:1) of their ED<sub>50</sub>'s values alone demonstrated synergism in both phases. This is important since the orofacial pain is a test not currently used in mice; the drugs are all analgesic for humans and phase II is representative of inflammatory pain. The synergism was: COX-3 > COX-2 > COX-1 inhibitors, this is particularly interesting since the inhibitor of COX-3, paracetamol, displayed a robust anti-inflammatory activity in an assay of acute and inflammatory pain that mimics