Carbachol interactions with nonsteroidal anti-inflammatory drugs

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The inhibition of cyclooxygenase enzymes by nonsteroidal anti-inflammatory drugs (NSAIDs) does not completely explain the antinociceptive efficacy of these agents. It is known that cholinergic agonists are antinociceptive, and this study evaluates the interactions between carbachol and some NSAIDs. Antinociceptive activity was evaluated in mice by the acetic acid writhing test. Dose-response curves were constructed for NSAIDs and carbachol, administered either intraperitoncally (i.p.) or intrathecally (i.t.). The interactions of carbachol with NSAIDs were evaluated by isobolographic analysis after the simultaneous administration of fixed proportions of carbachol with each NSAID. All of the drugs were more potent after spinal than after systemic administration. The combinations of NSAIDs and carbachol administered i.p. were supra-additive; however, the i.t. combinations were only additive. Isobolographic analysis of the coadministration of NSAIDs and carbachol and the fact that atropine