

Evaluation of new derivatives of Arylidene-2 (-3 chloro anilino) nicotinic acid hydrazide as anti-inflammatory and analgesic agents

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Background and Aims: Non-steroidal anti-inflammatory drugs (NSAIDs) are consumed in treatment of inflammation and pain in many conditions. New derivatives of Arylidene-2 (-3 chloro anilino) nicotinic acid hydrazide, were synthesized in order to be evaluated for anti-inflammatory and analgesic effects in vivo. New types synthesized based upon modulation the NSAIDs side effects as well as improving their safety profile.

Methods: Anti-nociceptive activity was assessed by acetic acid induced writhing response. The suspension test compounds administration (i.p.) intraperitoneally (1% v/v; 10 mg/kg), then 30 min after aqueous acetic acid solution (1% v/v; 10 mg/kg) was administered intraperitoneally, analgesic activity was recorded via counting the number of writhes during 30 min after acetic acid injection in mice, then analgesic activity was calculated using the following formula, % inhibition = [(control mean – test mean) / control mean] ×100 Anti-inflammatory activity was determined using carrageenan-induced edema test in the hindpaws of rats, carrageenan (0.1 mL of 1% w/v in saline) was injected subcutaneously in the rat footpads 1 h after i.p. administration of compounds. The increase in paw volume (0.5, 1, 2, 3 and 4 hours after carrageenan) is calculated as percentage compared with the basal volume.

Results: Among all of analogues, 4-pyr, 3-F and 3-(Ome) with (90%, 57% and 60% inhibition) had the most potent analgesic activity and the compounds 4-pyr, 3-Cl, 2,4(Ome)₂, 3-F and 3-(Ome) exhibited the most potent anti-inflammatory activity, (investigations showed no ulcerogenic effects).

Conclusions: We demonstrated that most of The derivatives synthesized of arylidene-2(-3chloro anilino) nicotinic acid hydrazides were able to reduce the AcOH induced constrictions in the mice and also exhibited anti-inflammatory activity ranging from moderate to good in comparison with Carboxymethyl cellulose (CMC) and Niflumic acid as the reference drugs.

Keywords: Anti-inflammation; Analgesia; Carrageenan; Writhing test