**EVALUATION OF 1,4-DIOXO-2-BUTENYL ARYL AMINE DERIVATIVES AS PROMISING ANTI-INFLAMMATORY DRUGS**

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**Introduction:** Inflammation is a response of the organism to an infection, trauma, or cellular stress, causing swelling, pain, redness, heat, and loss of function. Of these, the first noticed symptom is the pain, due to the discomfort that it may cause. Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat inflammatory pain, due to the prostaglandin synthesis inhibition *via* enzyme cyclooxygenase 2 (COX-2), but these drugs can cause several dangerous side effects. Dipyrone, for example, is used to treat pain and is metabolized *in vivo* into 4 metabolites, including 4-aminoantipyrine-4-AA. However, it is thought that this drug produces a very weak anti-inflammatory effect. **Objective:** To develop compounds that can improve the effectiveness in inhibit COX-2, trough the evaluation of 4 compounds containing the active 4-aminoantipyrine and 1,4-dioxobutenyl derivatives. **Method:** The anti-inflammatory and antihyperalgesic activities were determined *in vivo* in mice. For this, paw edema tests, leukocyte influx, writhing test and formalin test were used. Male Swiss mice, 18-30g, were distributed in the groups: Water (10 mL / kg); 4-aminoantipyrine (4-AA; 48 mg/kg); C1- Maleic acid, C2- Maleimide, C3- Maleic ester, C4- Diels-Alder adduct (48 mg/kg); Dipyrone (500 mg/kg) and Morphine (5 mg/kg), in the formalin test. After, the edema progression was evaluated at the intervals of 30, 60, 120 and 240 minutes, according to the variation of the volumes between the control paws and the treated. The leukocyte influx was evaluated at 240 minutes through the total and differential cell counts. The number of abdominal writhing was counted for 30 minutes after acetic acid 0,6% injection and the time of paw licking was recorded in two phases, neurogenic (0-5 minutes) and inflammatory (15-30 minutes). The experiments were approved by the CEUA (949/2018). Results were expressed as mean ± E.P.M., ANOVA and Bonferroni tests (P<0.05). **Results:** The analogues (C1 to C4) reduced the paw edema in the period of 60 min (0.066±0.012 mL) in 51.5%, 42.4%, 31.8%, 48.5%, respectively. The influx of polymorphonuclear leukocytes induced by carrageenan (2193.0 ± 308.9 cell/mm3) was increased when compared the animals that received saline (121.6 ± 19.8 cell/mm3), but only treatment with C3 (77.8%) and C4 (35.6%) reduced this response. In the writhing test, acetic acid induced 104.2 ± 3.5 abdominal writhing. The compound 4-AA was more effective (74.8± 5.6 writhing) when compared to dipyrone in the same dose and only compound C1 (71.0 ± 5.3) was effective in the writhing reduction. In the formalin assay, animals treated with morphine, dipyrone, C1 and C3, reduced paw licking duration in 95.2%, 84.1%, 45.8%, 36.2%, respectively, while animals which received water presented paw licking time of 31.5 ± 11.3s, in the first phase. In the second phase, the animals treated with water presented a paw licking time of 149.5 ± 20.9 s. The treatment with morphine reduced this effect by 99.8%. No paw licking was observed for the group treated with dipyrone. Pre-treatment with 4-AA (23.7%), C1 (43.3%), C2 (35.0%), C3 (61.5%) and C4 (66.7%) were effective in the paw licking reduction time. **Conclusion:** The compounds **C1** to **C4** decrease of inflammatory painand have antihyperalgesic. However, only the analogues **C3** and **C4** demonstrated anti-inflammatory activity. These molecules efficiency in reducing pain and inflammation might be related to the inhibition of enzyme COX activity, and consequently, prostaglandins.