PHARMACOLOGICAL CHARACTERIZATION OF THE ANALGESIC EFFICACY OF CR4056, A NOVEL IMIDAZOLINE-2 RECEPTOR LIGAND, IN THE RAT MONOSODIUM IODOACETATE MODEL OF OSTEOARTHRITIC PAIN.

Comi Eleonora[1,2], Ferrari Flora[1], Mauri Valeria[1], Catapano Luca[1], Lanza Marco[1], Caselli Gianfranco[1], and Rovati Lucio C.[1]

[1] Pharmacology & Toxicology Department, Rottapharm Biotech Srl, Monza (MI), ITALY
[2] PhD program in Neuroscience, XXIX PhD cycle, University of Milan-Bicocca, Monza (MI), ITALY

Introduction and aim:
Osteoarthritis (OA) is a degenerative chronic joint condition. Joint pain is the earliest symptom of OA and is driven by both nociceptive and neuropathic mechanisms. CR4056, an I_2 ligand, was previously reported to be effective in several animal models of inflammatory, neuropathic and postoperative pain.
Aim of this study was to evaluate the effect of CR4056 in the model of OA pain obtained by the injection of monosodium iodoacetate (MIA) into the knee joint of rats, which produces cartilage degeneration, mimicking the painful and structural components of human OA. Besides, MIA model is associated with an early phase neuropathy.
Methods:
OA was induced by a single intra-articular injection of 1 mg/50 μl MIA in the infrapatellar area of the right knee of male Wistar rats. Pain thresholds were evaluated as mechanical allodynia (automatic Von Frey tester) and mechanical hyperalgesia (PAM device) on day 1 before MIA injection and on day 7, 14 and 21 after MIA injection. CR4056 (2, 6, 20 mg/kg) and 10 mg/kg naproxen were administered orally, as single treatment on day 7 and as sub-chronic treatment from day 14 to day 21, once a day.
Results and conclusion:
6 and 20 mg/kg CR4056 induced a statistically significant anti-allodynic effect on T14 and T21, and a statistically significant anti-hyperalgesic effect at each time point (T7, T14, T21). The analgesic efficacy of naproxen was statistically significant after the sub-chronic treatment only. CR4056 could, therefore, represent a new highly effective treatment option for OA pain.