New lactam derivatives acting as H3 receptor ligands with potential for the treatment of pain

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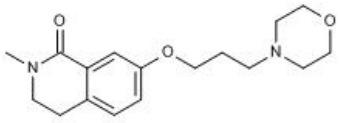
Among the four G protein-coupled receptors (H1-H4) identified as mediators of the biologic effects of histamine, the H3 receptor (H3R) is distinguished for its almost exclusive expression in the nervous system and the large variety of isoforms. H3Rs can modulate pain transmission by several mechanisms, and offer interesting therapeutic applications for the treatment of pain, in addition to Alzheimer's disease and other neurologic disorders. In a recent publication, researchers from HuaiHai Institute of Technology, in China, and colleagues, described the synthesis of a new series of **lactam derivatives acting as H3R ligands**. In vitro binding to H3 and H1 was evaluated. Optimization of structure-activity relationship led to the discovery of **[I]**, which showed the highest affinity and greatest selectivity for H3R. Acute toxicity testing of compound [I] showed a good safety profile at the highest dose (LD50 > 1000 mg/kg). In the formalin test in rats, the compound (1-10 mg/kg) exhibited dose-dependent antinociceptive effects. This compound emerges as a potential candidate for pain treatment (Dou, F. et al. Bioorg Med Chem Lett 2019, 29(12): 1492).



[I]