OPIOID ACTIVITY OF NEW CARBONYL DERIVATIVES OF 1-ARYL-2-AMINOIMIDAZOLINE-2

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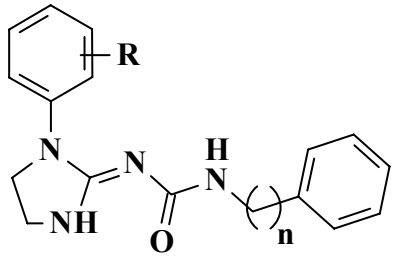
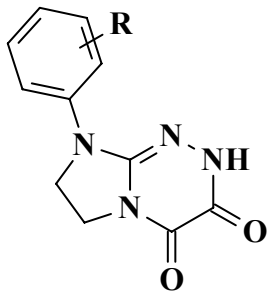
The carbonyl derivatives of 1-aryl-2-aminoimidazoline-2 both chain and fused structure were found to have significant antinociceptive activity connected with activation of the MOP (mu opioid protein) receptor [1-3]. The analyze of their structures allowed formation of non-classical MOP agonist pharmacophor [1,3]. Recent results on the chain (imidazole-2-yl)urea (**A**) and imidazo[2,1-c][1,2,4]triazine (**B**) [4] derivatives are implementing the model with new features, which have to be taken under consideration in planning further synthesis.



n = 1,2

A



B

Series **A** compounds exhibited significant antinociceptive activity in the "writhing test", reversed by small dose (5 mg kg^{-1} i.p.) of naloxon. Antinociceptive activity of series **B** compounds depended on the substituent in the N8-phenyl ring location and the tautomeric keto-enol equilibrium shift toward the 3-oxo form. Compounds existing predominantly in 3-hydroxy form do not show any antinociceptive activity and their serotonergic activity is strongly increased.

[1] D. Matosiuk, S. Fidecka, L. Antkiewicz-Michaluk, I. Dybała, A. E. Kozioł, *Eur. J. Med. Chem.* **2001**, 36 783.
[2] D. Matosiuk, S. Fidecka, L. Antkiewicz-Michaluk, J. Lipkowski, I. Dybała, A. E. Kozioł, *Eur. J. Med. Chem.* **2002**, 37 761.
[3] D. Matosiuk, S. Fidecka, L. Antkiewicz-Michaluk, I. Dybała, A. E. Kozioł, *Eur. J. Med. Chem.* **2002**, 37 845.
[4] K. Sztanke, S. Fidecka, E. Kędzierska, Z. Karczmarzyk, K. Pihlaja, D. Matosiuk, *Eur. J. Med. Chem.* **2005**, 40, 127.