PP25. ACUTE TOXICITY AND ANALGESIC ACTIVITY OF SOME1,2,3,4-TETRAHYDROISOQUINOLINE DERIVATIVES IN THE ACETYLCHOLINE WRITHING TEST

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Nowadays, it was shown that, according to the latest SOS clinical study, the risk of myocardial infarction development was not limited to coxibs, but also well-known NSAIDs, such as ketoprofen, nimesulide, meloxicam, naproxen, ibuprofen, diclofenac, indomethacin, ketorolac may have such side effects [1]. Actual problem of medicinal chemistry and pharmacology is the search for safer new candidate substances with analgesic action.

In this work, the acute toxicity of four new 1,2,3,4-tetrahydroisoquinolines was studied. The test substances were administered orally to 18-22 g mice using a non- traumatic metal probe at doses ranging from 1000.0 to 13000.0 mg/kg. Each dose was tested on 6 mice. The mean lethal dose was determined by the well-known method of Litchfield and Wilcoxon. The acetylcholine writhings were induced by intraperitoneal administration of acetylcholine at a dose of 3.2 mg/kg, which leads to the appearanceof the "writhing" syndrome. Each group included 6 mice. The test substances wereadministered subcutaneously to the experimental group of mice for 15 minutes before the introduction of acetylcholine, and the number of "writhings" for 20 minutes counted.

It was shown that the acute toxicity of compounds is lower than the toxicity of the reference drug ketoprofen by 3-3.5 times, respectively. The studied compounds at doses of 1–5 mg/kg in the acetylcholine writhing test showed a pronounced analgesic effect, which, however, was inferior to that of ketoprofen. Further study of the analgesic action of 1,2,3,4-tetrahydroisoquinolines is of current interest.

REFERENCES

[1] Castellsague J, Riera-Guardia N, Calingaert B, et al. Drug Saf. 2012;35. pp.1127– 1146.