

## STUDY ON THE INFLUENCE OF POTENT INHIBITORS OF NEURONAL NITRIC OXIDE SYNTHASE ON THE ANTINOCICEPTIVE AND ANTICONVULSANT ACTIVITY OF BENZODIAZEPINES IN MICE

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The influence of 1-(2-trifluoromethylphenyl)imidazole (TRIM) and 3-bromo-7-nitroindazole (3-Br-7-NI), potent and relatively selective inhibitors of neuronal nitric oxide (NO) synthase, on the antinociceptive and anticonvulsive effects of diazepam and clonazepam was investigated in mice. The effects were assessed in the writhing test and pentetrazole-induced seizures, respectively. The antinociceptive effects of the threshold doses of diazepam (1 mg/kg) and clonazepam (0.0375 mg/kg) were significantly increased by TRIM (7.5 mg/kg) but not by 3-Br-7-NI (10 mg/kg). L-arginine (125 mg/kg) was able to reverse the effects produced by co-administration of TRIM (7.5 mg/kg) with diazepam (1 mg/kg), and also of TRIM (7.5 mg/kg) with clonazepam (0.0375 mg/kg). Protective efficacy of the threshold dose (0.05 mg/kg) of diazepam against pentetrazole-induced tonic convulsions and death was significantly increased by TRIM (25 mg/kg) but not by 3-Br-7-NI (10 and 100 mg/kg). TRIM (25 mg/kg) intensified the protective efficacy of the threshold dose (0.005 mg/kg) of clonazepam, but the effect was not reversed by L-arginine (125 mg/kg). The present results seem to confirm, at least partly, participation of NO in antinociceptive and anticonvulsant effects of benzodiazepines, and point to TRIM as a better tool than 3-Br-7-NI for examination of the role of NO in behavioral studies.

**Key words:** diazepam, clonazepam, 1-(2-trifluoromethylphenyl)imidazole (TRIM), 3-bromo-7-nitroindazole (3-Br-7-NI), nociception, seizures, mice

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