**Pharmacological Reports**
2007, 59, 467–473
ISSN 1734-1140



**Short communication**

# Effect of $N^G$-nitro-L-arginine on the anticonvulsant action of four second-generation antiepileptic drugs in pentetrazole-induced clonic seizures in mice

Jarogniew J. Łuszczki[1], Marcin Szadkowski[2], Stanisław J. Czuczwar[1,3]

[1]Department of Pathophysiology, Medical University of Lublin, Jaczewskiego 8, PL 20-090 Lublin, Poland

[2]First Department of Internal Medicine with Dialysis Station, County Hospital in Starachowice, Radomska 70, PL 27-200 Starachowice, Poland

[3]Department of Physiopathology, Institute of Agricultural Medicine, Jaczewskiego 2, PL 20-950 Lublin, Poland

**Correspondence:** Jarogniew J. Łuszczki, e-mail: jarogniew.luszczki@am.lublin.pl

**Abstract:**
The exact role of compounds modulating nitric oxide (NO) content in the brain during seizure phenomena is under intensive investigation. This study was aimed at determining the effect of $N^G$-nitro-L-arginine (L-NA; a non-selective NO synthase inhibitor) on the anticonvulsant activity of four second-generation antiepileptic drugs (AEDs: gabapentin [GBP], oxcarbazepine [OXC], tiagabine [TGB] and vigabatrin [VGB]) in the mouse pentetrazole (PTZ)-induced seizure model. The acute adverse-effect liability of the studied AEDs in combinations with L-NA were evaluated in the chimney test (motor coordination).
Results indicate that L-NA (40 mg/kg; *ip*) significantly reduced the anticonvulsant activity of OXC in the PTZ test, by increasing its $ED_{50}$ from 20.9 to 29.8 mg/kg ($p < 0.05$). Similarly, L-NA at doses of 20 and 40 mg/kg considerably attenuated the antiseizure effects of VGB by raising its $ED_{50}$ from 595 to 930 mg/kg ($p < 0.05$), and 1022 mg/kg ($p < 0.01$), respectively. L-NA at lower doses of 10 and 20 mg/kg did not affect significantly the anticonvulsant effects of VGB and OXC in PTZ-induced seizures. Likewise, the co-administration of L-NA (40 mg/kg; *ip*) with GBP and TGB was associated with no significant changes in their anticonvulsant activities in PTZ-induced seizures in mice. Moreover, none of the examined combinations of L-NA (40 mg/kg; *ip*) and second-generation AEDs (at their $ED_{50}$ values) affected motor coordination in the chimney test.
Based on this preclinical study, one can conclude that L-NA reduced the anticonvulsant activities of VGB and OXC in the mouse PTZ-induced seizure model. Only, GBP and TGB were resistant to the action of L-NA in this model.

**Key words:**
$N^G$-nitro-L-arginine, nitric oxide, oxcarbazepine, vigabatrin, pentetrazole-induced seizures, tiagabine, gabapentin, mice