Abstract:
The efficacy of lamotrigine and felbamate against maximal electroshock (MES)-induced seizures was assessed under conditions mimicking the pharmacoresistance associated with an increased excitatory neurotransmission. N-methyl-D-aspartate (NMDA), but not kainate applied at subconvulsive dose, reduced the activity of lamotrigine against MES-induced seizures increasing its ED₅₀ value from 4.3 (3.2–5.6) to 6.1 (5.2–7.2) mg/kg (p < 0.001). This effect was reversed by co-application of an NMDA receptor antagonist D-(E)-2-amino-4-methyl-5-phosphono-3-pentenoic acid (CGP 40116) at 0.1 mg/kg [4.5 (3.7–5.6) vs. 6.1 (5.2–7.2) mg/kg; p < 0.001]. The anticonvulsive action of felbamate was altered by neither NMDA nor kainate. In conclusion, the data presented here indicate that felbamate, but not lamotrigine, effectively prevents generalized tonic-clonic seizures, also when NMDA-mediated neurotransmission is enhanced. The impaired antiepileptic potential of lamotrigine might be restored in such scenario by the co-administration of a very low dose of NMDA receptor antagonist.

Key words:
epilepsy, pharmacoresistance, glutamate receptors, lamotrigine, felbamate