Anticonvulsant and antidepressant activity of the selected terpene GABA derivatives in experimental tests in mice

Monika Kubacka¹, Tadeusz Librowski¹, Ryszard Czarnecki¹, Bożena Frąckowiak², Stanisław Lochyński²

¹Department of Pharmacodynamics, Faculty of Pharmacy, Medical College, Jagiellonian University, Medyczna 9, PL 30-688 Kraków, Poland
²Institute of Organic Chemistry, Biochemistry and Biotechnology, Wrocław University of Technology, Wybrzeże Wyspiańskiego 27, PL 50-370 Wroclaw, Poland

Correspondence: Tadeusz Librowski, e-mail: mllibrow@cyf-kr.edu.pl

Abstract:
The present study was designed to investigate the central nervous system activity of terpene GABA (and piracetam) derivatives designated as BF-1, BF-2, BF-3, BF-4, BF-5, BF-6. We assessed their anticonvulsant activity in the two main mouse models of seizures (MES-test, PTZ-test), an antidepressant-like effect in the forced swim test (FST), as well as an influence on spontaneous locomotor activity. Our study demonstrated the strong anticonvulsant activity of (1S,3R,7R)-(−)-3,8,8-trimethyl-4-aza-bicyclo[5.1.0]acetate-5-one hydrochloride (compound BF-2) in the PTZ-test. Activity of BF-2 was equipotent to ethosuximide (380 mg/kg, po) in the PTZ-test, when used at a dose of 100 mg/kg, po. No neurotoxic effects were demonstrated by administration of all tested compounds. Moreover, BF-2, BF-3, BF-6 compounds significantly reduced the immobility time in FST at both doses (by 21–50%), while BF-5 induced a significant anti-immobility effect only when used at a dose of 100 mg/kg (by 39%). The compound BF-6 used at the dose of 30 mg/kg was the most active (50% reduction), and the effect was similar to the result obtained with classical antidepressant – imipramine. The motor stimulatory activity was demonstrated by BF-1 compound at the dose of 100 mg/kg with no effect at a lower (30 mg/kg) dose. On the other hand, the BF-3 at 30 mg/kg significantly decreased spontaneous activity during 30 min observation period, while no alteration in this activity during 6-min observation was detected. At present, it is not possible to indicate which mechanisms of novel, active terpene GABA derivatives are involved in the demonstrated antidepressant-like activity. Although further studies are needed to solve this issue, these data suggest a potential value of the examined terpene GABA derivatives.

Key words:
GABA, terpenes, anticonvulsant-, antidepressant-like activity, mice