Pharmacological Reports
2012, 64, 102–112
ISSN 1734-1140

Analgesic and anticonvulsant activity of new derivatives of 2-substituted 4-hydroxybutanamides in mice

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Abstract:
Earlier *in vitro* studies of the compounds marked as GT27, GT28, GT29 and BM128 revealed their inhibitory action towards murine γ-aminobutyric acid (GABA) transporters (mGAT1–mGAT4). In the present paper, the pharmacological activity of four γ-hydroxybutyric acid (GHB) amide derivatives was investigated. The following procedures were involved: locomotor activity, hot plate and electroconvulsive threshold tests. The compounds' influence on motor coordination was evaluated in the chimney test, as well. Intraperitoneal (*ip*) administration of the GHB derivatives decreased animals' locomotor activity (ED_{50} values ranged between 23.79 and 26.37 mg/kg). At a dose of 25 mg/kg (*ip*) the compounds prolonged the nociceptive reaction time latency in the hot plate assay to various degree and GT28 and GT29 were the most potent ones in this respect. Their analgesic efficacy was particularly pronounced 30 min after their administration [percent of maximal possible effect (%MPE) = 16.93 and 22.72, respectively]. The investigated GHB derivatives, except for GT29 at 100 mg/kg, increased the electroconvulsive threshold by approximately 4–11 mA as compared to the vehicle-treated mice. In the chimney test they impaired the animals' motor coordination to various degree. We suggest further investigations of the compounds to estimate their biological activity.

Key words:
electroconvulsive threshold, GABA uptake inhibitors, hot plate, mice, motor coordination, tiagabine, tonic hind limb extension