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# GET73 modulates rat hippocampal glutamate transmission: evidence for a functional interaction with $mGluR_5$

Luca Ferraro[1], Sarah Beggiato[1], Maria Cristina Tomasini[1], Tiziana Antonelli[1], Antonella Loche[2], Sergio Tanganelli[1]

[1]Department of Clinical and Experimental Medicine, Pharmacology Section and LTTA Centre, University of Ferrara, Via Fossato di Mortara 17-19, 44100, Ferrara, Italy

[2]Laboratorio Farmaceutico CT, Via Dante Alighieri 71, 18038, Sanremo, Italy

**Correspondence:** Luca Ferraro, e-mail: frl@unife.it

**Abstract:**
In the present study, the effects of the γ-hydroxybutyrate (GHB) analog GET73 on hippocampal glutamate transmission have been evaluated by an approach combining *in vivo* microdialysis with the *in vitro* evaluation of tissue slices. The microdialysis results indicated that local perfusion (60 min) with 10 nM – 1 mM GET73 increased extracellular glutamate levels in the CA1 region of the hippocampus of freely moving rats in a concentration dependent manner. In tissue slices from the rat hippocampus, GET73 (1 μM – 10 μM) did not affect L-[$^3$H]glutamate uptake, whereas treatment with 1 μM GET73 significantly increased $K^+$-evoked, but not spontaneous, glutamate efflux. The GHB analog did not affect the increase in glutamate efflux induced by 100 μM and 300 μM NMDA. In contrast, 500 nM GET73, a concentration at which it is ineffective alone, partially but significantly counteracted the increase in $K^+$-evoked glutamate efflux induced by 100 μM CHPG, an mGluR5 agonist. When 500 nM GET73 was coperfused with 100 μM MPEP, it amplified the decrease in $K^+$-evoked glutamate efflux induced by the mGluR5 antagonist. Interestingly, the increase in $K^+$-evoked glutamate efflux induced by 1 μM GET73 was counteracted by coperfusion with a low (10 μM) concentration of MPEP, which by itself is ineffective. Finally, 500 nM GET73 did not affect the reduction of $K^+$-evoked glutamate efflux induced by the mGluR2/3 agonist LY379268.
These findings demonstrate that the GHB analog GET73 significantly affects glutamate transmission in the hippocampus, and its profile of action differs from that of its parent compound.

**Key words:**
CA1 hippocampus slices, glutamate efflux, mGluR5 antagonist, γ-hydroxybutyrate