Bioavailability Studies and in vitro Profiling of the Selective Excitatory Amino Acid Transporter Subtype 1 (EAAT1) Inhibitor UCPH-102 - DTU Orbit (09/11/2017)

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Although the selective excitatory amino acid transporter subtype 1 (EAAT1) inhibitor UCPH-101 has become a standard pharmacological tool compound for in vitro and ex vivo studies in the EAAT research field, its inability to penetrate the blood–brain barrier makes it unsuitable for in vivo studies. In the present study, per os (p.o.) administration (40 mg kg−1) of the closely related analogue UCPH-102 in rats yielded respective plasma and brain concentrations of 10.5 and 6.67 μm after 1 h. Three analogue series were designed and synthesized to improve the bioavailability profile of UCPH-102, but none displayed substantially improved properties in this respect. In vitro profiling of UCPH-102 (10 μm) at 51 central nervous system targets in radioligand binding assays strongly suggests that the compound is completely selective for EAAT1. Finally, in a rodent locomotor model, p.o. administration of UCPH-102 (20 mg kg−1) did not induce acute effects or any visible changes in behavior.

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