

NEW TORASEMIDE DERIVATIVES INHIBIT BRAIN SLICES AND
ASTROCYTES SWELLING INDUCED BY POTASSIUM.

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K⁺-enriched media induce brain cells swelling as found in hypoxic, ischemic or hypoglycemic brain edema. The K⁺-induced swelling is essentially located into the glia and presumably secondary to the activation of the Na⁺/K⁺/2Cl⁻ cotransport system, as suggested by its specific decrease by furosemide (FS). Torasemide (TS) is known to have the same mechanism of action in kidney and erythrocytes. New synthesized torasemide derivatives, with a higher liposolubility, have been tested on K⁺-induced brain swelling. 50mM K⁺-induced brain swelling was determined in adult rat brain slices incubated in presence of FS, TS and new lipophilic derivatives BM4, BM9 and JDL 364. Results showed a significant reduction of slices swelling by 1mM JDL 364 (25 %), 1mM FS (33 %), 0.1mM BM4 (45 %) and 0.1mM BM9 (56 %). 1mM TS had no effect. FS, TS and JDL 364 were also tested on 50mM K⁺-induced astrocytic swelling, determined by the ¹⁴C-3-O-methylglucose cellular space of newborn rat astrocytes cultures (21 days old, DBcAMP free medium). All three compounds (1mM) showed a significant reduction of swelling : FS (50 %), TS (78 %) and JDL 364 (100 %). These results show that new torasemide lipophilic derivatives inhibit K⁺-induced swelling of brain slices and cultured astrocytes. The in vivo antiedematous properties of these compounds remain to be assessed in hypoxic brain edema. (Supported by a grant from Carlo-Erba Farmitalia).