

21st Scientific Symposium of the Austrian Pharmacological Society:
Joint Meeting with the British Pharmacological Society and the
Pharmacological Societies of Croatia, Serbia and Slovenia
Graz, 16–18 September 2015

MEETING ABSTRACT

A2.24

Quercetin uptake into neonatal rat astrocytes

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Background: Quercetin is a flavonoid widely distributed in fruits and vegetables, and is a potent antioxidant with neuroprotective activity. In animal transgenic models of Alzheimer's disease, quercetin decreased astrogliosis and microgliosis in the hippocampus and the amygdala. The open question remains if the quercetin activity on astrocytes is extracellular or intracellular. Thus, the aim of this study was to investigate the uptake of quercetin into astrocytes.

Methods: We isolated astrocytes from the cerebral cortex of neonatal rats, and grown them into monolayer cultures. We determined the time dependence and concentration dependence of [³H]quercetin uptake into the cultured astrocytes at 37 °C (total uptake) and at 4 °C (non-specific uptake). To study the role of membrane proteins, we pre-incubated the cells with PMSF and DTNB, which form an irreversible link in the active site of membrane proteins with serine and cysteine, respectively. To study the energetic role of uptake, we (i) inhibited the respiratory chain by pre-incubation with KCN, NaN₃ and NaVO₃; and (ii) inhibited glycolysis by pre-incubation with NaF. We also studied the involvement of OATPs (organic anion-transporting polypeptides) and SGLT1 (sodium-dependent glucose co-transporter 1) transporters in the uptake of [³H]quercetin by co-incubation with their substrates or inhibitors.

Results: We found that the uptake of quercetin is mediated by facilitated diffusion by comparing the uptake at 37 °C and at 4 °C, where we have obtained no kinetic differences ($K_m = 4,5 \mu\text{M}$; $V_{\text{max}} = 94 \text{ pmol/mg protein/min}$). The inhibition of the cell energy production in astrocytes did not affect the uptake of quercetin, thus confirming that there is no active transport. The transport was inhibited by PMSF and DTNB pre-incubation, showing the importance of membrane proteins. Moreover, we showed that both OATPs and SGLT1 are involved in the uptake of quercetin.

Discussion: Uptake of quercetin is mediated by facilitated diffusion involving several membrane transporter systems. Our study opens the perspective of studying flavonoid-mediated neuroprotective activity by focusing on astrocytes and other glial cells.

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