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Quercetin inhibits glucose transport by binding to an exofacial site on GLUT1

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Abstract

Quercetin, a common dietary flavone, is a competitive inhibitor of glucose uptake and is also thought to be transported into cells by GLUT1. In this study, we confirm that quercetin is a competitive inhibitor of GLUT1 and also demonstrate that newly synthesized compounds, WZB-117 and BAY-876 are robust inhibitors of GLUT1 in L929 cells. To measure quercetin interaction with L929 cells, we develop a new fluorescent assay using flow cytometry. The binding of quercetin and its inhibitory effects on 2-deoxyglucose (2DG) uptake showed nearly identical dose dependent effects, with both having maximum effects between 50 and 100 μ M and similar half maximum effects at 8.9 and 8.5 μ M respectively. The interaction of quercetin was rapid with $t_{1/2}$ of 54 seconds and the onset and loss of its inhibitory effects on 2DG uptake were equally fast. This suggests that either quercetin is simply binding to surface GLUT1 or its transport in and out of the cell reaches equilibrium very quickly. If quercetin is transported, the co-incubation of quercetin with other glucose inhibitors should block quercetin uptake. However, we observed that WZB-117, an exofacial binding inhibitor of GLUT1 reduced quercetin interaction, while cytochalasin B, an endofacial binding inhibitor, enhanced quercetin interaction, and BAY-876 had no effect on quercetin interaction. Taken together, these data are more consistent with quercetin simply binding to GLUT1, but not actually being transported into L929 cells via the glucose channel in GLUT1.

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