Silybin and dehydrosilybin decrease glucose uptake by inhibiting GLUT proteins.

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Source

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Abstract

Silybin, the major flavonoid of Silybum marianum, is widely used to treat liver diseases such as hepatocellular carcinoma and cirrhosis-associated insulin resistance. Research so far has focused on its anti-oxidant properties. Here, we demonstrate that silybin and its derivative dehydrosilybin inhibit glucose uptake in several model systems. Both flavonoids dose-dependently reduce basal and insulin-dependent glucose uptake of 3T3-L1 adipocytes, with dehydrosilybin showing significantly stronger inhibition. However, insulin signaling was not impaired, and immunofluorescence and subcellular fractionation showed that insulin-induced translocation of GLUT4 to the plasma membrane is also unchanged. Likewise, hexokinase activity was not affected suggesting that silybin and dehydrosilybin interfere directly with glucose transport across the PM. Expression of GLUT4 in CHO cells counteracted the inhibition of glucose uptake by both flavonoids. Moreover, treatment of CHO cells with silybin and dehydrosilybin reduced cell viability which was partially rescued by GLUT4 expression. Kinetic analysis revealed that silybin and dehydrosilybin inhibit GLUT4-mediated glucose transport in a competitive manner with K(i)=60 and 116 µM, respectively. We conclude that silybin and dehydrosilybin inhibit cellular glucose uptake by directly interacting with GLUT transporters. Glucose starvation offers a novel explanation for the anti-cancer effects of silybin.