Epidermal growth factor receptor mediates silibinin-induced cytotoxicity in a rat glioma cell line.


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Abstract

Silibinin, derived from milk thistle extract, has been shown to inhibit growth factor receptor-mediated mitogenic and cell survival signaling, and to alter cell cycle regulators. Alteration in pathways regulating cell growth likely account for silibinin's inhibition of tumor growth. Since the epidermal growth factor receptor (EGFR) is a key regulator in cell signaling pathways, in the present study we directly tested the hypothesis that the EGFR plays a key role in mediating silibinin cytotoxicity to cancer cells. We generated a cell line, 9L-EGFR, which stably expressed human EGFR; the parental rat glioma cell line, 9L, does not contain endogenous EGFR message or protein. Our results show that expression of EGFR was both necessary and sufficient for conferring toxicity in response to silibinin in 9L-EGFR cells. Addition of silibinin was shown to inhibit EGFR activation by EGF in 9L-EGFR cells. These studies support the hypothesis that silibinin toxicity to cancer cells involves the EGFR signaling pathway. The findings presented here provide a rationale for understanding the growth inhibition effect of silibinin in cancer cells, and warrant further investigation into the effect of silibinin on specific pathways of cell signaling mediated by the EGFR receptor.

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PMID: 14614320