



A presurgical study of oral silybin-phosphatidylcholine in patients with early breast cancer.

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Abstract

Silybin-phosphatidylcholine is an orally bioavailable complex of silybin, a polyphenolic flavonolignan derived from milk thistle, endowed with potential anti-cancer activity in preclinical models. The purpose of this window of opportunity trial was to determine, for the first time in early breast cancer (BC) patients, the breast tissue distribution of silybin. Twelve BC patients received silybin-phosphatidylcholine, 2.8 g daily for 4 weeks prior to surgery. Silybin levels were measured before (SIL) and after (TOT-SIL) enzymatic hydrolysis by HPLC-MS/MS in biological samples (plasma, urine, BC and surrounding normal tissue). Fasting blood samples were taken at baseline, before the last administration and 2 hours later. All patients were fully compliant and completed the treatment program. No toxicity was observed. SIL and TOT-SIL were undetectable in baseline samples. Despite a high between-subject variability, repeated administration of Siliphos achieved levels of TOT-SIL of 31121 to 7654 ng/mL in the plasma, and up to 1375 ng/g in BC tissue. SIL concentrations ranged from 10861 to 1818 ng/mL in plasma and up to 177 ng/g in BC tissue. Median TOT-SIL concentration was higher in the tumor as compared to the adjacent normal tissue ($P=0.018$). No significant change in either blood levels of IGF-I and nitric oxide, or Ki-67 in tumors was noted. Silybin-phosphatidylcholine, taken orally, can deliver high blood concentrations of silybin which selectively accumulates in breast tumor tissue. These findings provide the basis for a future phase II biomarker trial in breast cancer prevention.

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