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Dietary flaxseed lignan or oil combined with tamoxifen treatment affects MCF-7 tumor growth through estrogen receptor- and growth factor-signaling pathways.

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Abstract

This study aimed to elucidate which component of flaxseed, i.e. secoisolariciresinol diglucoside (SDG) lignan or flaxseed oil (FO), makes tamoxifen (TAM) more effective in reducing growth of established estrogen receptor positive breast tumors (MCF-7) at low circulating estrogen levels, and potential mechanisms of action. In a 2 x 2 factorial design, ovariectomized athymic mice with established tumors were treated for 8 wk with TAM together with basal diet (control), or basal diet supplemented with SDG (1 g/kg diet), FO (38.5 g/kg diet), or combined SDG and FO. SDG and FO were at levels in 10% flaxseed diet. Palpable tumors were monitored and after animal sacrifice, analyzed for cell proliferation, apoptosis, ER-mediated (ER-alpha, ER-beta, trefoil factor 1, cyclin D1, progesterone receptor, AIBI), growth factor-mediated (epidermal growth factor receptor, human epidermal growth factor receptor-2, insulin-like growth factor receptor-1, phosphorylated mitogen activated protein kinase, PAKT, BCL2) signaling pathways and angiogenesis (vascular endothelial growth factor). All treatments reduced the growth of TAM-treated tumors by reducing cell proliferation, expression of genes, and proteins involved in the ER- and growth factor-mediated signaling pathways with FO having the greatest effect in increasing apoptosis compared with TAM treatment alone. SDG and FO reduced the growth of TAM-treated tumors but FO was more effective. The mechanisms involve both the ER- and growth factor-signaling pathways.

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