

DIETITIANS' NEWS

Flax and Its Mammalian Lignans Inhibit Tumour Angiogenesis in Mice

by Diane H. Morris

In a recent mouse study, flax and its mammalian lignans, enterodiol and enterolactone, exerted potent antiestrogenic effects on estrogen receptor-positive (ER+) breast cancer by inhibiting tumour growth and angiogenesis.¹ Angiogenesis – the formation of new blood vessels – is an essential step in tumour development and metastasis. A tumour's ability to form new blood vessels depends on a delicate balance of factors that promote or inhibit angiogenesis. One potent promoter of angiogenesis is vascular endothelial growth factor (VEGF).² High tumour levels of VEGF have been associated with a poor prognosis and decreased survival among patients with breast cancer.¹

Using both *in vitro* and *in vivo* methods, Jungeström and colleagues at the University Hospital in Linköping, Sweden and the University of Toronto in Canada reported that milled flax, enterodiol and enterolactone counteract the tumour growth-promoting effects of estradiol and decrease both angiogenesis and VEGF secretion.¹ The main lignan in flax, secoisolariciresinol diglucoside (SDG), is converted to the mammalian lignans enterodiol and enterolactone by gut bacteria.³

The *in vivo* model mimicked breast cancer in premenopausal women by maintaining a stable background level of estrogen. For the *in vivo* study, nude mice were implanted with estradiol pellets, injected with MCF-7 cells and fed a basal diet until tumours formed. When tumours reached a size of ~30 mm², one group continued the basal diet (control group), one group started a 10% milled flax diet, one group started with daily injections of enterodiol, and one group started with daily injections of enterolactone. Final tumour weights were significantly lower in the milled flax, enterodiol and enterolactone groups compared with the control group. VEGF secreted by tumours decreased by ~50% and angiogenesis decreased by ~60-80% in the treatment groups compared with the control group.

This study shows that milled flax and its mammalian lignans can inhibit tumour growth through their actions on estradiol and angiogenesis in ER+ breast cancer *in vivo*. The flax and mammalian lignans acted by blocking two actions of estradiol – its ability to increase the expression (activation) of VEGF receptor 2 and also its ability to increase VEGF secretion. The flax and mammalian lignans reduced VEGF receptor 2 expression and decreased VEGF secretion, while also inhibiting angiogenesis and tumour growth, all without exhibiting estrogen-like actions themselves. These findings suggest ways in which flax and its lignans may help prevent ER+ breast cancer in humans.

References

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