

*****11/12/2002 - A diet rich in flaxseed seems to reduce the size, aggressiveness and severity of tumours in mice that have been genetically engineered to develop prostate cancer, according to new research from Duke University Medical Center in the US. And in 3 per cent of the mice, the flaxseed diet kept them from getting the disease at all, report the researchers.**

"We are cautiously optimistic about these findings," said Wendy Demark-Wahnefried, associate professor at the division of urology and senior author of the study. *"The amount of flaxseed given to each mouse was 5 per cent of its total food intake, which would be a very difficult amount for humans to eat, but it does signal that we are on the right track and need to continue research in this area."*

According to Demark-Wahnefried, planned clinical trials must be completed before it can be concluded that dietary flaxseed protects against prostate cancer in humans. Clinical studies by other researchers have suggested that dietary fibre reduces cancer risk, and omega-3 fatty acids also have shown a protective benefit against cancer. Flaxseed, which is high in fibre, is the richest plant source of omega-3 fatty acids. It is also a source of lignan, a specific family of fibre-related compounds that appear to play a role in influencing both oestrogen and testosterone metabolism. Since testosterone may be important in the progression of prostate cancer, lignan could help inhibit the growth and development of the disease.

In the Duke study, 135 mice genetically engineered to develop prostate cancer were divided into a control group and an experimental group. The experimental group received a regular mouse diet, but 5 per cent of the diet was in the form of flaxseed. Half of the mice in both groups were fed their respective diets for 20 weeks and the remainder for 30 weeks. At the 20- and 30-week end points, the mice were autopsied to check for tumour growth and progression of the disease to other organs.

"Tumours in the untreated control group were twice the size of tumours in the flaxseed group," said Dr Xu Lin, research associate, division of urology and lead author of the study. *"The tumours were also less aggressive in the flaxseed group, and two of the mice in the flaxseed group did not develop prostate cancer at all. The rates of apoptosis (tumor cell death) were also higher in the flaxseed group. And while it was not statistically significant, the flaxseed group had fewer rates of the cancer spreading to other organs."* While the results are promising, the researchers say they are not surprising. The study is the third in a series by the Duke Medical Center researchers to show the benefits of flaxseed in reducing the growth and development of prostate cancer.

The first study, published in July 2001 in *Urology*, demonstrated that a low-fat diet supplemented with flaxseed was associated with slower tumour growth. In this pilot study, 25 men with prostate cancer began adding ground flaxseed to their diets for 34 days. At the end of the study, the men saw a drop in testosterone levels and a trend toward lower prostate specific antigen (PSA) levels, a marker for prostate cancer. The diet also was tolerated well and gave the authors hope for this dietary intervention. The second study, published in the November-December 2001 issue of *Anticancer*

Research, examined the effect lignans have on prostate cancer cell lines. This study showed that flaxseed-derived lignans inhibited the growth of three distinct human prostate cancer cell lines through hormonally dependent and independent mechanisms. "So far we have observed the suppression of prostate cancer in humans, mice and at the cellular level," said Lin. "It's not a fluke or a coincidence. It's an encouraging line of research."

Demark-Wahnefried added: "Our results are encouraging. However, before we can truly state that flaxseed is beneficial in humans, larger well-controlled trials are needed. The National Cancer Institute has provided us with the support to conduct a randomised clinical trial in 160 men with prostate cancer that will examine whether a low-fat diet, flaxseed supplementation or a combination of low-fat diet and flaxseed supplementation will be most effective in stopping prostate cancer cells from dividing. That trial is currently under way." The latest research is published in the November 2002 issue of *Urology*, and was sponsored by the National Institute on Aging, the National Cancer Institute and the Committee for Urologic Research Education and Development at Duke University Medical Center.



Flax Seed May Prevent Growth of Prostate Cancer

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June 5, 2007 (Chicago) — Flaxseed supplementation significantly reduced tumor proliferation rates in prostate cancer patients in a trial reported here at the American Society of Clinical Oncology (ASCO) 43rd Annual Meeting. "These results demonstrate that flaxseed may well protect against prostate cancer growth," said lead researcher Wendy Demark-Wahnefried, PhD, from Duke University Medical Center, in Durham, North Carolina. "But this is just the first study," she added. "We will need to replicate the results before we can make recommendations."

The study was highlighted in an ASCO press conference and was also discussed at 2 overview sessions during the meeting. "It is very provocative," commented Bruce Cheson, MD, from the Lombardi Comprehensive Cancer Center and Georgetown University Hospital, in Washington, DC. "There is a hint of something there," he told journalists when moderating the press briefing.

However, all of the experts highlighting the finding emphasized that further research is needed.

The study was funded by grants from the National Cancer Institute and National Institutes of Health, and the ground flaxseed was donated by ENRECO, Inc. The dose was 30 g/day, which is about 3 round tablespoons, and the ground flaxseed was mixed with food and drink. "On its own, ground flax seed has a mild nutty taste," Dr. Demark-Wahnefried commented. Flaxseed is one of the richest sources of lignan, which has several activities that could be useful in cancer, she explained. Lignan affects androgen metabolism, has antimitotic and antioxidant activity, has an impact on the eicosanoid milieu, and is a rich source of omega-3 fatty acids.

The researchers also investigated the role of a low-fat diet (with fat contributing less than 20% of the total energy) in the same study. As a result, the trial had 4 groups: placebo control, flaxseed, low-fat diet, and the combination of low-fat diet with flaxseed. It was conducted in 161 patients scheduled for a prostatectomy, and the median age of 59 years was lower than that of the average prostate cancer patient (68 years), Dr. Demark-Wahnefried commented. Men participated in the study for a mean duration of 30 days and then underwent surgery; the removed tissue was sent to 2 pathologists for analysis.

A primary analysis showed a significant reduction in the mean tumor proliferation rate in the 2 groups on flaxseed ($P = .0013$), and a reduction that was not statistically significant in the group just on the low-fat diet ($P = .053$). (The figures presented at the meeting are based on reports from both pathologists and differ from the figures in the abstract, which

were from only 1 report available at the time it was written, Dr. Demark-Wahnefried explained.)

These results suggests that the cancer cells were growing at a significantly slower rate (roughly 30% to 40% slower) in the 2 groups taking flaxseed than in the group on placebo or on the low-fat diet alone, she added. The finding fits in with previous research conducted in vitro, which showed that lignan slowed the rate of growth of prostate cancer cells, she noted.

Mean Tumor Proliferation Rates

Control	Flaxseed	Low-Fat Diet	Flaxseed Plus Low-Fat Diet
3.23	1.66	2.56	1.55

Secondary analyses, which included prostate cancer apoptosis and histology of benign tissue, showed no significant differences between the groups, but the patients on the low-fat diet showed — unsurprisingly — a significant reduction in serum cholesterol, she said.

In answer to a question from the audience, Dr. Demark-Wahnefried noted that the greatest effect of flaxseed was seen in men with the lower Gleason score (< 7, in 68% of the men) and hence milder disease, which is "what you would expect." She hesitated, however, over questions about mechanism of action behind the effect seen, noting that there was no reduction in testosterone, which had been expected. There may be an effect of omega-3 fatty acids on how the cancer cells stick together, and lignan may also have antiangiogenic properties and deprive the tumor of its blood supply, but further work is needed on the mechanisms involved. "We also need to disentangle the effect of flaxseed from that of the low-fat diet," she added.

"We are excited that this study showed that flaxseed is safe and associated with a protective effect on prostate cancer," Dr. Demark-Wahnefried said. The results are "compelling, but preliminary," she added, noting that her team is now planning another trial.

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