Technology Licensing Opportunity

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Flaxseed Lignan-Enriched Complex Products in Chronic Disease

Natural Health Product

- **Potential use in several chronic diseases**
- **Identification of metabolite and novel method of action**

Available for Collaboration

Principal Inventor:

Dr. Jane Alcorn
Professor
College of Pharmacy
& Nutrition
University of Saskatchewan

Industry Collaborators:
Archer Daniels Midland

Funding:
Saskatchewan Health Research Foundation

Publications:

- Preclinical data published in Br J Nutr, J Nat Prod, Nat Prod J.
- Safety evaluation published in Pharmaceut Biol.
- Publications associated with human preclinical data and clinical trials are in preparation and ready for submission in early 2016.

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Benefits of flax lignans: Lignans are naturally occurring biologically active polyphenolic compounds present in flaxseed. The major lignan in flaxseed is SDG (Secoisolariciresinol diglucoside) and flaxseed is the richest known source of this compound (Fig.1). Cell models, animal studies, epidemiological studies, and randomized human clinical trials have all demonstrated significant potential for flaxseed lignan supplementation in management of or risk reduction for a number of chronic diseases including cancer, heart disease, BPH, hypertension, and inflammatory bowel disease.

History of Industry Engagement: In 2007 Archer Daniels Midland (ADM) began marketing a flaxseed lignan enriched complex (38% SDG) called BeneFlax® with both FDA and Health Canada approval. Later, ADM stopped production of BeneFlax® to focus on soy isoflavanoids. However there has been a growing body of science to support the value of lignan supplementation in management of chronic diseases. Bioactive enriched products like BeneFlax® are likely to show meaningful therapeutic or chemopreventative properties.

Commercial Opportunity: Archer Daniels Midland has expressed a willingness to work with any company interested in resuming production of BeneFlax®. We are seeking the interest of investors to revive the technology and resume production of BeneFlax® or a BeneFlax® like product. We believe that the market is now more receptive to this product than it was 8 years ago and the new science including the current studies at the University of Saskatchewan supports an expanded range of uses for BeneFlax® including as a sole therapeutic, an adjuvant therapy, or chemopreventative for chronic disease such as risk factors for cardiovascular disease (e.g. hypercholesterolemia, hypertension) and inflammatory conditions of the gastrointestinal tract, such as inflammatory bowel disease.

Fig 1.

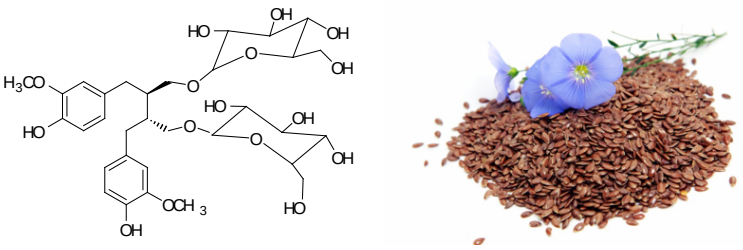

Figure 1. A. The principal flaxseed lignan, Secoisolariciresinol Diglucoside. B. Flax plant and seeds

Collaborators: Dr. Alcorn has built a strong collaborative network of researchers and clinician researchers including Dr. Ed Krol (Pharmacy and Nutrition, Dr. Phil Chilibeck (Kinesiology), Dr. Susan Whiting (Pharmacy and Nutrition), Dr. Sharyle Fowler (Medicine), and Dr. Thomas Hadjistavropoulos (U. of Regina), as well as with one of the original inventors of the technology for BeneFlax, Dr. Alister Muir, to create an integrated package of safety, efficacy, and mechanism of action data for the lignans of flaxseed.

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Pre clinical Data: In Dr. Alcorn's laboratory, animal model studies demonstrate clear anticholesterolemic effects and in vitro analyses may have identified lignan mode of action (a novel mechanism) in the hypercholesterolemic effect of lignans (results pending). Furthermore, in vitro analyses are demonstrating important effects in inflammatory conditions of the gastrointestinal tract. (Fig 2) As well, in in vitro evaluations we have we demonstrated synergism between the lignans and important chemotherapeutic agents used in treatment of breast or prostate cancer (Table 1).

Fig. 2

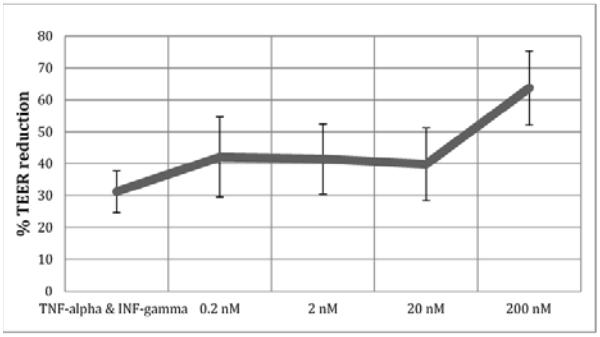

Figure 2 . Protective effect of the flaxseed lignan metabolite, enterolactone, on a polarized intestinal epithelium (HCT-8) after 48 hours of co-incubation with inflammatory stimulus (TNF-alpha/Interferon-beta). Data represents mean ± S.D of n= 3.

Table 1

PC3	Drug only	Plus Met A		Plus Met B	
		25 µM	50 µM	25 µM	50 µM
Cabazitaxel IC_{50} pM	1168	732	310	295	162
95% CI	728-1870	373-1437	195-491	193-453	94-280
Docetaxel IC_{50} pM	936	627	374	238	92
95% CI	563-1556	275-1427	180-776	122-462	35-241
Doxorubicin IC_{50} nM	200	178	159	138	69
95%CI	140-284	119-265	95-267	72-262	18-259

Table 1. IC_{50} values of cabazitaxel, docetaxel, and doxorubicin in combination with different concentrations of flax lignan metabolites, Metabolite A and Metabolite B in prostate cancer cell line (PC3). Data are reported as mean (n=3) IC_{50} values with 95% confidence interval (CI). Combination with lignans decreased the IC_{50} values of chemotherapeutic drugs via a concentration-dependent manner.

Clinical Data: Recently completed Phase IIa human clinical trials in healthy and frail older adults indicate good safety and tolerability of BeneFlax®. Current human clinical trials are underway to examine efficacy of BeneFlax® oral supplementation in patients with 1) mild-to-moderate ulcerative colitis and 2) elderly patients with high normal to stage I hypertension. Furthermore, a validated pharmaceutical analytical method has allowed for important pharmacokinetic (PK) characterizations of the flaxseed lignans (e.g. intestinal permeability in Caco-2, phase II metabolism in intestinal and hepatic microsomes, cytochrome P450 inhibition potential (DDI potential), PK of individual flaxseed lignans in animal models, PK of single oral dose and multiple oral dose administration of BeneFlax® in healthy adults (Fig. 3)). The combination of our biomedical studies on safety, efficacy, and mechanism of action, and clinical trials to confirm the biomedical studies, has compiled important information to begin to establish a scientific basis for possible health claims for the flaxseed lignans.

Fig. 3

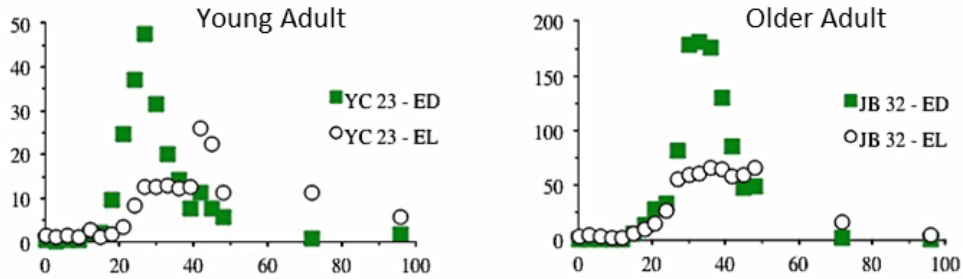

Figure 3. Single oral dose administration of BeneFlax® (equivalent to 300 mg secoisolariciresinol diglucoside) to young and elderly healthy adults. Age-dependent differences in lignan pharmacokinetics were noted.

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