U.S. Food and Drug Administration, National Center for Toxicological Research:
Safety and Bioactivity of Estrogenic Dietary Supplements

Americans of all ages can be exposed to potent estrogenic compounds in dietary supplements, foods, and drugs, but many of the products are specifically marketed to older individuals, such as menopausal or postmenopausal women for their perceived health benefits and potential to relieve menopausal symptoms. This research project has critically investigated the role of dose, target tissue, and life stage timing of exposure in producing physiological effects, because both beneficial and detrimental effects are possible in mammary, adipose tissue, and the central nervous system.

Lead Agency:

U.S. Department of Health and Human Services, U.S. Food and Drug Administration, National Center for Toxicological Research (NCTR)

Agency Mission:

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

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Partner Agencies:

University of Illinois – CRADA (Cooperative Research and Development Agreement)

General Description:

The overall goal of this project has been to evaluate the safety and bioactivity of estrogenic dietary supplements. The component projects are aimed collectively at defining the activity of estrogenic dietary supplements in various target tissues (including mammary gland, adipose tissue, and central nervous system) in which estrogens are known to have diverse – sometimes beneficial and sometimes detrimental – effects. All

of the investigations were also designed to critically evaluate the important issue of safety, which with hormonal agents such as estrogens is typically complex, because it depends on dosage and exposure, metabolism, and age, and often can vary from target tissue to target tissue. Americans of all ages are exposed to these potent estrogenic compounds, but many of the products are specifically marketed to older individuals, such as menopausal or postmenopausal women for their perceived health benefits and potential to relieve menopausal symptoms. Therefore, the research has focused in particular on the benefits and risks from the use of these products by older individuals.

Excellence: What makes this project exceptional?

The overall goal of this research project was to evaluate the safety and bioactivity of estrogenic dietary supplements through the combined effort of several experienced investigators, who have a long-standing track record of scientific excellence and well-developed collaboration among them. Together, these investigators have organized a series of interdependent research projects that collectively are aimed at defining the activity of estrogenic dietary supplements in mammary, adipose tissue, and the central nervous system, in which estrogens are known to have diverse effects.

Significance: How is this research relevant to older persons, populations and/or an aging society?

The FDA has severely limited regulatory authority over dietary supplements, and, as a result, the safety and efficacy of most of these products are unknown. A significant proportion of the estrogenic dietary supplements currently on the market contain soy isoflavones. Many of the beneficial effects of isoflavones are associated with their estrogenic action. This presents a paradox -- because dietary estrogens, like endogenous and hormone-replacement therapy, have both potential risks and benefits. Many of these products are specifically marketed to older individuals, particularly menopausal or postmenopausal women for their perceived health benefits and potential to relieve menopausal symptoms. Based on research from this project in appropriate animal models, consumption of dietary estrogens could affect growth of estrogen-dependent breast cancer, the development of adipose tissue and obesity, and affect cognitive function in the elderly.

Effectiveness: What is the impact and/or application of this research to older persons?

These studies contain important direct estrogenic comparisons of effects from purified isoflavones, which occur in dietary supplements, with more complex soy ingredients that occur in whole-soy foods and other commercial products. In this way, critical guidance can be provided to older Americans about the healthiest practices regarding consumption of soy-based products.

Innovativeness: Why is this research exciting and newsworthy?

Breast cancer is the second leading cause of cancer death in U.S. women, most breast cancer cases (~75%) occur in postmenopausal women, and most (~70%) are estrogen-dependent. The stimulatory effect of estrogens on the growth of breast cancers can be blocked by two manipulations: competitive binding interactions at the estrogen receptor (ER) by anti-estrogens like tamoxifen, and competitive inhibition of estrogen synthesis by aromatase inhibitors. These adjuvant endocrine therapies have proven to be highly effective and have led to significant improvements in survival for postmenopausal women with early-stage estrogen-dependent breast cancer. This research project has shown that dietary soy isoflavones can negate the inhibitory effects of tamoxifen and aromatase inhibitors on the growth of human breast tumors in a mouse xenograft model. These studies suggest that such diet-drug interactions have the potential to reduce the effectiveness of frontline endocrine therapy for breast cancer in postmenopausal women.