Preclinical Toxicology Studies

To assess the safety of this product and confirm that it is non-toxic when consumed, a risk assessment framework has been designed according to the estimated level of exposure. This includes acute toxicity, repeat-dose chronic toxicity and mutagenicity tests. Safety on acute ingestion has been established based on acute oral toxicity studies. These studies revealed that the combined botanical extracts did not cause any significant clinical signs and necropsy findings in doses up to 2g/kg. No deaths were reported; hence the LD50 could not be quantified.

Similarly, the extracts did not cause any clinically significant findings in haematology, blood chemistry, urinalysis or histopathology of systemic targets in the repeat-dose chronic toxicity studies which simulate the effects of long term exposure. In addition in genotoxicity tests, the botanical extracts did not cause any in vivo chromosomal genetic DNA mutation.

Clinical Efficacy of fxmenopause

In the 2003 UK study on the effects of **fxmenopause** on menopausal women, an exposure-response relationship was established. Trial participants recorded an average 50% and 66% baseline reduction in hot flashes or night sweats within 10 days and 3 weeks of consumption of **fxmenopause**, respectively. The percent reduction is well beyond the 25-30% reduction usually attributed to placebo. Overall, there was a significant improvement of total symptom scores measured using the MRS, RAND 36, PIRS and Facial Skin Questionnaire among the trial participants, leading to an enhanced quality of life.

Background Scientific & Biomedical Information

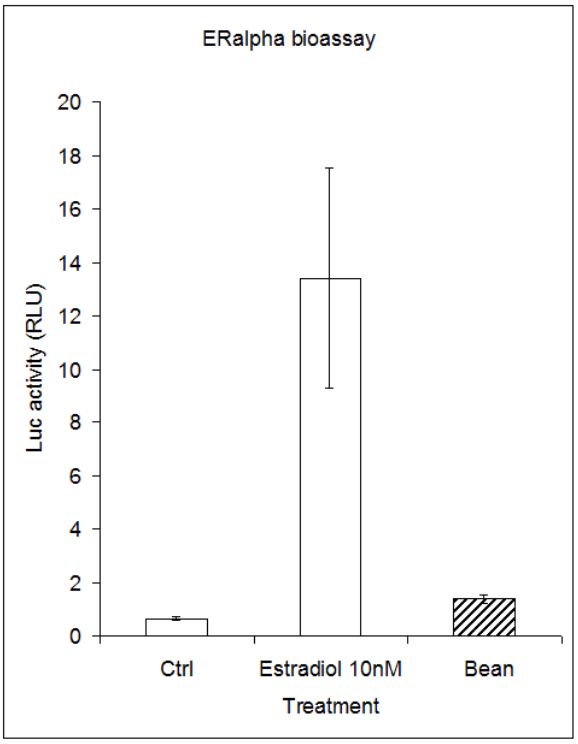
The human oestrogen receptor has two isoforms alpha and beta. Both isoforms are responsible for mediating the physiological actions of oestrogens such as estradiol in humans, particularly women. The oestrogen receptor plays a vital role in many aspects of human biology such as bone density, collagen synthesis, menstrual cycle, primary and secondary female phenotypic characteristics such as breast development, body fat etc. Consequently, either hypo (too low) oestrogen or hyper (too high) oestrogen levels can contribute to disorders such as osteoporosis and breast cancer respectively.

Phytoestrogens are naturally occurring compounds from plants that possess the ability to modulate the human oestrogen receptor isoforms and consequently exert beneficial biological effects (Murkies et. al, 1998). Phytoestrogens actually refers to a group of polycyclic compounds that include isoflavones, flavones and lignans that occur naturally in legumes, fruits and herbs.

The term 'modulate' refers to the ability to either augment (enhance) or attenuate (reduce) activity. For example, if the oestrogen receptors are saturated with the physiological or synthetic oestrogens (PSE) that cause hyperactivity, these phytoestrogens may compete with and displace these PSE. Some phytoestrogens are weaker activators of oestrogen receptor than PSE and therefore exert a moderating effect on oestrogen receptor activity. Such effects would be desirable in cases where hyper levels of oestrogens may pose health risk such as breast and uterine cancers (Lamartiniere et. al., 2002; Pagliacci et. al.; 1994). On the other hand, hypogonadal conditions such as menopause which portends lower oestrogen levels and predisposes the individual to osteoporosis and other attendant health conditions may benefit from the supplemental effects of phytoestrogens that help to offset lower levels of physiological oestrogens in the body (Erdman et. al., 2000). In other words, phytoestrogens are a class of natural selective oestrogen receptor modulators (SERMs).

However, different phytoestrogenic plant extracts may contain other undesirable co-extracted compounds. For example, phytoestrogenic Dong Quai also contains coumarins, a blood thinner. Black Cohosh besides having phytoestrogenic effects, also exert hypotensive effects. In addition, different classes of phytoestrogens can preferentially activate the oestrogen receptors isoforms alpha or beta to a different degree and preliminary scientific research suggest this phenomena may support the body in distinct aspects such as cardiovascular health, breast cancer etc (Singer et. al., 2002; Lazennec et. al., 2001). Therefore, the choice of extracting phytoestrogens from the botanical source is important.

fxmenopause is a unique dual formulation of two food sourced phytoestrogens. The bean phytoestrogen has unique SERM activity that preferentially activates the oestrogen receptor beta to a greater extent relative to the oestrogen receptor alpha (Please refer to Figure 1).



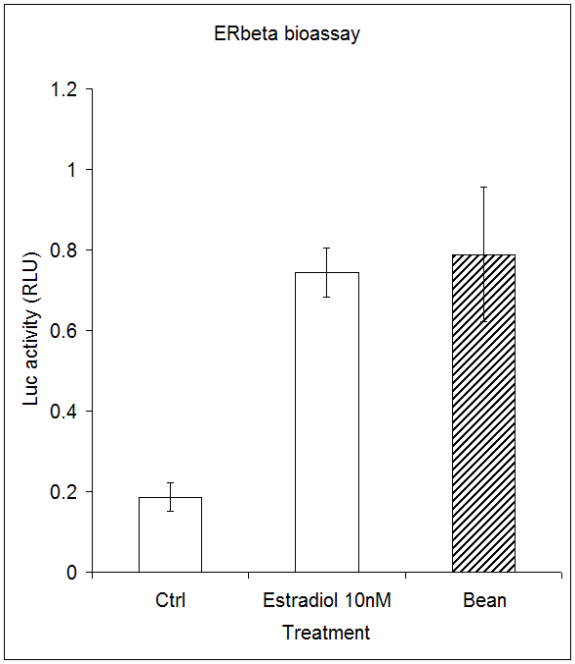


Figure 1. Selective modulation of the oestrogen receptors (ER) alpha and beta.

Graph A shows weak agonistic activity of the bean (right striped bar) relative to the physiological oestrogen, estradiol (middle white bar) on the ER alpha.
Graph B indicates that the bean (right striped bar) is an efficient activator of the ER beta with respect to estradiol (middle white bar).

In addition, **fxmenopause's** formulation has comprehensive in-vitro studies that demonstrate its biological ability to synergistically enhance or boost oestrogen receptors in the presence of their cognate ligands, the oestrogens (Figure 3).

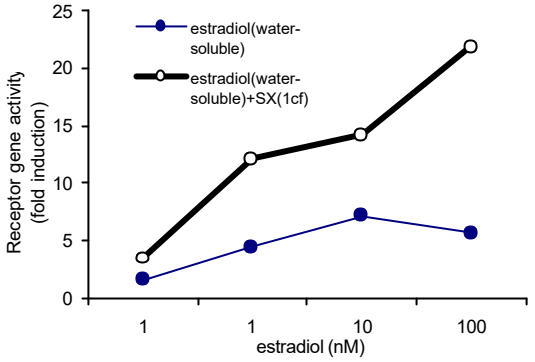


Figure 2. Synergistic augmentation of oestrogen receptor (ER) in the presence of its cognate ligand, estradiol.

Phytoestrogens are natural anti-oxidants per se because of their polycyclic structure. Antioxidants are also incurring a great deal of interest as emerging data in free oxygen radical research suggests that cellular and molecular oxidative damage in vivo may play a fundamental role in the ageing process and associated conditions such as cardiovascular damage, cancer risk and neurodegenerative diseases. Dietary phytoestrogens may also support optimal skin condition as human oestrogen receptors play a role in collagen synthesis and cellular growth.

FXMenopause is specifically formulated to provide dietary phytoestrogenic support in adult women only.

The role of **fxmenopause's** beans in the menopause years and beyond has been positively assessed by the UK Food Standards Agency in compliance with regulation EC 1924/2006 relating to nutrition and health claims made on food. Under this regulation, any food product claiming to have a health or nutritional benefit is required to be supported by science and meet a list of European Commission approved wording.

References:

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