Science FAQ Questions

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1. What are oestrogen receptors and why are they important for women?

Oestrogen receptors are functional proteins in the human body that detect the presence of female steroid hormones called oestrogens. They act biologically on many aspects of the woman's body such as skin, collagen and connective tissues, breast development, reproductive functions, bone and muscle metabolism, cardiovascular and cerebral function, sex drive (libido) and psychological well-being. Hence, low female hormone (oestrogens) levels can lead to weak oestrogen receptor action. Lack of oestrogen receptor activities will then negatively affect many of the above-mentioned tissues and organs.

2. What are phytoestrogens?

Phytoestrogens refer to metabolites found naturally in certain plants and they are actually a wide range of different compounds such as isoflavones, lignans and coumarins. These plant metabolites are NOT steroids but they can still interact with the oestrogen receptors in the woman's body. Interestingly, clinical and scientific studies carried out in Japan, the United States and many other countries have shown that phytoestrogens interact with the oestrogen receptors differently from both the human oestrogens and the synthetic analogues. Phytoestrogens have been suggested to have a protective effect against some forms of breast cancer, ovarian cancer etc. Yet at the same time, phytoestrogens can support cardiovascular function, optimal skin condition and assist in the relief of hot flushes and other climacteric symptoms.

3. What is the difference between synthetic and physiological oestrogens, and phytoestrogens?

Both synthetic and physiological oestrogens are steroids. In fact, 17ß estradiol and/or synthetic derivatives containing the tetracyclic ring system are derived via the mevalonate and deoxyxylulose phosphate pathways with cholesterol as precursor. On the other hand, phytoestrogens are derived via the shikimate pathway. Cinnamic acids precursors lead to lignans. Examples include enterolactone and enterodiol. Isoflavonoids derived from flavanones include daidzein and genistein. In other words, phytoestrogens consists of diverse chemical classes structurally distinct from steroids.

In terms of biological properties, phytoestrogens such as genistein have pleotropic effects. For example, genistein not only binds to the oestrogen receptors (ERs) but is also a competitive inhibitor of tyrosine kinase (TK). TK is a key signal transduction enzyme involved in phosphorylation cascade and plays a role in cell growth and mitosis. Cancer researchers are interested in TK role in promoting carcinogenesis and metastasis of neoplastic cells. In contrast, estradiol is not known to be an inhibitor of TK. In fact, c-fos/c-jun phosphorylation cascade induced by estradiol activation of ER alpha leads to proliferation of oestrogen sensitive cells. Oestrogens and phytoestrogens do not share the same chemical nor biological properties.

4. Do oestrogen receptors exert any side-effects on the human body?

Ostrogen receptors (ERs) are not known to exert side-effects per se in the human body. Only mutated ERs and/or inappropriate regulation (hypo or hyper) are implicated in any disorders having ERs as etiological factors. As further advances in genomics and proteomics are made, we are increasingly aware of pharmacogenomic differences between individuals. In other words, optimal oestrogen doses may vary between patients. 1nM estradiol serum level may be optimal for individual A but the same dose may lead to over-activation of individual B's ERs as individual B may possess a more sensitive receptor due to polymorphism in her ER encoding gene or even downstream ER responsive genes.

On the other hand, specific types of phytoestrogens modulate the ER isoforms differentially. Some phytoestrogens are very weak agonist, some are strong oestrogen mimetic and some are even natural selective oestrogen receptor modulators (SERMs) (such as **fxmenopause**). A weak ER agonist will not adequately suppress climacteric symptoms but will certainly widen therapeutic index. Hence, the need for adjuvants that will complement the key pharmacologic compound in exerting therapeutic relief. A simple oestrogen/progesterone formula will inevitably fail to achieve this balance. Whereas, a complex formula, particularly from plants, would permit an array of molecular pathways to be modulated, thereby allowing for weaker ER activation that can be compensated via other effectors not involving the ERs. In other words, not only the ER-based mechanism is involved, but also anti-inflammatory pathways such as COX-2 and glucocorticoid receptor (GR) can be harnessed to address the problem of climacteric vasomotor symptoms such as night sweats and hot flushes.

5. Is it true that only cognate ligands that can fit spatially into the tertiary conformational pocket of the apo-LBD of the ERs can exert an agonist or antagonist effect?

In the old paradigm, only cognate ligands that can fit spatially into the tertiary conformational pocket of the apo-LBD of the ERs can exert an agonist or antagonist effect. In the presence of an agonist binding to the steroid receptor, these PAs will synergistically enhance the holo-receptor transactivational function on hormone responsive genes. In hypo-oestrogen conditions such as menopause; low oestrogen levels or conversely, weak phytoestrogenic effect can be boosted via the PAs. This supports ER activity without the need for excessive high doses of oestrogens or phytoestrogens. This then negates the potential side-effects associated with high doses of oestrogenic chemicals (synthetic or plant-based), such as DVT (associated with oestrogen use) or bleeding (associated with some phytoestrogens such as coumarin). These patents pending phytoaugmenters are trademarked and are integral components of the **fxmenopause** formula.

6. Do both oestrogens or phytoestrogens share the same reported or anecdotal adverse effects?

Historically and now clinically, oestrogens used in conventional HRT (cHRT) have been reported to be associated with a myriad of side-effects such as cancer risks, thrombosis and even cardiovascular problems. In the same vein, a number of similar theoretical risks have also been attributed to phytoestrogens (PEs) and more importantly, vegetative foods containing phytoestrogens on the assumptions that PEs are oestrogen mimetics. In fact, epidemiological studies clearly suggest that diets (such as traditional Japanese or Chinese meals) rich in phytoestrogens protect against cancers and a host of other chronic diseases.

However, animal studies using isolated or single phytoestrogen such as genistein at mega-doses have demonstrated that oestrogen-sensitive tumour growths were increased in vivo and hence the many health warnings that PEs may be as dangerous as oestrogens used in cHRT. On the other hand, PEs such as enterolactone and enterodiol have been implicated in lowering breast cancers amongst vegetarians. A seeming paradox.

On closer analysis, plants (and hence plant-derived supplements such as **fxmenopause**) do not just contain a single type of PE or even a whole lot of PEs. They (the plants) contain a variety of other phytochemicals, such as the ones that may be useful in modulating COX-2 or GR, so on and forth. Specific plants may even contain indole-3-carbinole (shown in some studies to have anti-cancer effect) or naturally occurring anti-oxidants which further contribute to the overall health benefits imparted to the consumer. Current pharmaceuticals such as ethical drugs used in cHRT certainly do not provide such adjuvant benefits. Therefore, a botanical supplement such as **fxmenopause**, carefully researched and well formulated using specific plant extracts can confer both the efficacy required for the specific clinical condition in question as well as conferring collateral health benefits.

Clearly, to ignore the various epidemiological studies of Eastern cultures where cancers and even menopausal symptoms are less prevalent in PE rich diets vs the recent clinical studies implicating cHRT in health risks would be closing ourselves to the benefits that can be derived from botanical therapeutics. Particularly, ones that are scientifically researched but selectively formulated from traditional natural remedies such as **fxmenopause**.

7. Are hot flushes, mood swings and night sweats due solely to lack of holo-ER activity?

Vasomotor symptoms such as hot flushes and night sweats plus psychological disturbances such as mood swings associated with the climacteric are not due entirely to lack of ER activity. Otherwise, all postmenopausal women will continue to experience these symptoms. That is clearly not the case, clinically and anecdotally speaking. The period of hormonal changes, where oestrogen synthesis is gradually reduced and the negative feedback mechanism between the hypothalamus-pituitary-gonadal axis trigger off increased FSH, LH production plus many other endocrinological changes. These changes lead to consequent biochemical cascades within the body. These biochemical processes trigger off associated physiologic disturbances such pro-inflammatory responses (partially contributing to hot flushes etc) involving cytokines and prostaglandins etc.

Hence, a botanical supplement such as **fxmenopause** which contains specific phytochemicals that can modulate other key molecular effectors in these perturbed processes (such as COX-2 mediated prostaglandin synthesis) will be able to alleviate the global menopausal symptoms, without relying on relatively high doses of oestrogens/oestrogen mimetics (PEs included) that works only via the ER pathway. Hence, the therapeutic index for an advanced, scientifically formulated supplement like **fxmenopause** will be wider than that of a singular drug entity. On the other hand, many current health supplements for menopause rely on traditional herbal information only, but partially using conventional drug development principle and end up using only a single herbal ingredient (which again narrows the therapeutic index). Or, using an empirical mixture of herbs without specific scientifically proven functions, which does not really differ from the traditional holistic paradigm of herbal medicines (such as TCM and Ayurvedic).

In contrast, **fxmenopause** was researched and developed using a convergence principle, where the fields of molecular genetics, pharmaceutical technologies and natural remedies are specifically and selectively converged. This allows fxmenopause to achieve the broad therapeutic benefits of plant remedies without sacrificing the cognitive science and technology that underpins modern mainstream medicine and pharmaceuticals.