

Selective estrogen receptor beta agonists mechanism of action and clinical applications in women's health and cancer

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Estrogens effects are mediated through two estrogen receptor (ER) subtypes, ER α and ER β . Estrogens are the most commonly prescribed drugs to treat menopausal conditions. Estrogens non-selectively trigger both ER α and ER β pathways in tissues resulting in both beneficial and adverse effects. To overcome the adverse effects it is necessary to understand the differential gene regulation and the biological responses of the two ER subtypes as well as their cross-talk. ER subtype drugs that are also tissue selective may result in more specific and safer therapies.

Animal studies demonstrated that ER α and ER β selective drugs produce different biological effects. These findings demonstrate that a new therapeutic approach to treating diseases and symptoms associated with Women's health and menopause could develop with drugs that selectively regulate ER α or ER β signaling pathways. We discovered three classes of ER β -selective compounds; ER β binders, ER β activators and ER β binder/activator. ER β -selective compounds might be clinically useful for treating hot flashes and inflammatory conditions associated with menopause, such as atrophic vaginitis, weight gain and osteoporosis. ER β -selective compounds might also be beneficial for the prevention and treatment of breast cancer. Bionovo's Menerba is entering Phase 3 clinical testing for the treatment of menopausal hot flashes after successful results in a randomized double blind Phase 2 clinical trial. Bionovo's Seala is entering Phase 1-2 clinical testing for atrophic vaginitis, and multiple other compounds are tested for additional pro-inflammatory conditions. ER β -selective agonists might provide a new generation of safer drugs for preventing and treating menopausal conditions and breast cancer. An important and critical understanding of the biological- physiological role of ER β is still needed.