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Natural and Synthetic Estrogens Regulate Human Health

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Introduction

Estrogen are very important chemical compounds very essential for our body functions. The cholesterol, what we eat through food, gets converted by the action of various enzymes. Scientists have synthesized estrogenic molecules in the laboratory and used them for oral contraceptives and other therapeutic purposes. Environmental estrogenic molecules (xenestrogen) played havocs in human life. Plants also make estrogenic substances (phytoestrogen); they are very useful for mankind. All steroid hormones. estrogen are synthesized including from cholesterol through common precursor steroid, pregnenolone which is formed by the enzymatic cleavage of a 6-carbon side-chain of the 27-carbon cholesterol molecule. Cholesterol is a starting substance of group of estrogenic compounds [1]. On the other hand, synthetic estrogen are compounds obtained by chemical synthesis that possess estrogenic activity [2]. In addition to these compounds there estrogenic are estrogenic action mimicking compounds known as xenestrogen and phytoestrogen (Figure 1).

Figure 1: comparison of structures of natural estradiol (E2) and synthetic estrogen diethylstilbesterol (DES) and ethinyl estradiol (EE2).

Estrogen

Estrogen are a category of sex steroid hormones; they are the most essential hormones in the human body responsible for the proliferation, development and regulation of the female reproductive system. Though these are present in males also in minute quantities, they are primarily responsible for development of secondary sex characteristics [3]. There are three majors endogenous estrogen that have estrogenic hormonal activity namely, estrone (E1), estradiol (E2), and estriol (E3). Estrone, estradiol and estriol all work at different strengths in the body, with estradiol being the most potent followed by estrone and

then estriol. Just as they work at different potencies, they are each also beneficial for different processes in our bodies (Figure 2). Estriol: a weak oestrogen and a minor female sex hormone. Levels of estriol in women who are not pregnant are almost undetectable Estriol promotes the uterus' growth and gradually prepares a woman's body for giving birth Levels of estriol start to rise during the eighth week of pregnancy [3].

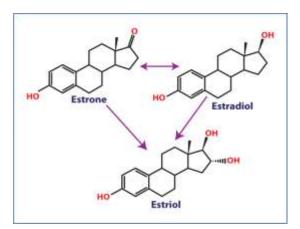


Figure 2: Among 3 estrgenic hormones estradiol is most important one, however, when there is demand for estriol rest 2 can be converted to estriol. Estradiol; is a major steroid hormone mainly produced by granulose cells of the ovaries. It is responsible for breast development, reproductive health and other female characteristics. It affects in pictogram levels. The quantities of this hormone vary due to age, sex, and health history of an individual. In premenopausal females, normal estradiol levels are 30 to 400 pg/ml. In postmenopausal females, normal estradiol levels are 0 to 30 pg/ml. Estrone: comes from the ovaries, as well as the adipose tissue and adrenal glands. It is a weaker estrogen, commonly found in higher quantities in postmenopausal women. Estrone is used in intramuscular and vaginal formulations, and is used as an estrogen in the treatment of symptoms of low estrogen levels such as hot flashes and vaginal atrophy in postmenopausal women. Estrogens responsible for many of the body's functions, regulating a woman's journey through puberty, fertility and menopause. Estrogens are helping

control: Body temperature, Muscle maintenance, Healthy sleep, Blood flow, Collagen levels in your skin, Memory function, Mood, Concentration, Libido (Sex Drive), Bone density. Estrogen Changes Over Time; Estrogen is incredibly important and as we get production decreases naturally, eventually leading to menopause, characterised by dramatically low levels of estrogen. However, many women will experience hormonal conditions which are caused or exacerbated by estrogen deficiency or an excess (compared to proge sterone) in their system. Symptoms of low estrogen can even include anxiety and low mood, which are also associated with menopause but can happen whenever the body is going through hormone withdrawal.

Synthetic Estrogens

Natural estrgens are produced in the body by the ovaries, fatty tissue and adrenal. whereas synthetic estrogens are synthesized in the laboratory with chemicals. They also possess estrogenic activity. One such compound is ethinyl estradiol (EE2). the synthetic estrogen diethylstilbesterol These compounds are used inoral contraceptives and as postmenopausal hormone therapy. New data suggest that these exposures induce epigenetic modifications in the mammary gland and germ cells, thereby causing an inheritable increase in breast cancer risk for multiple generations. Maternal exposure to during pregnancy increases breast cancer risk in both exposed mothers and their daughters.

Xenestrogen

Xenestrogen act like endocrine disruptors since they mimic the estrgens itself. And are found in water, aie and a variety of everyday items, that is why they are also known as environmental estrogens [4]. Xenestrogen are a sub-category of the endocrine disruptor group that specifically have estrogen-like effects (Figure 3). Endocrine disruptors are a category of chemicals that alter the normal function of hormones. Normally, our endocrine system **DOI:** https://doi.org/10.36811/jca.2020.110007

releases hormones that signal different tissues telling them what to do. When chemicals from the outside get into our bodies, they have the ability to mimic our natural hormones; blocking or binding hormone receptors. This is particularly detrimental to hormone sensitive organs like the uterus and the breast, the immune and neurological systems, as well as human development [5].

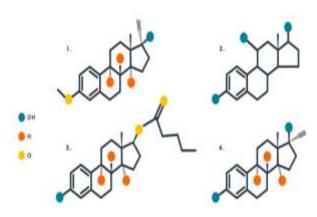


Figure 3: Structure-activity relationships for a large diverse set of natural, synthetic, and environmental estrogens> The diagram shows that by changing (OH), (H) or (O) groups their activity also changes.

Phytestrogen

"Phyto-" (plant) estrogen works similar like animal estrogen in humans, is a female hormone that regulates functions in both women and men. Phytestrogen, though plantbased, work as endocrine disruptors same way as xenoestrogens. But they are not as harmful as xenoestrogen. When we eat phytoestrogen, our bodies may respond as if our own estrogen were present [6]. A plant-based diet is very rich in natural phytoestrogen in healthy amounts, especially from soy. A high intake of phytoestrogen may disrupt the body's hormonal balance. Use of phytoestrogen is not associated with increased an risk of endometrial cancer or breast cancer.

Applications of Estrogens

Estrogens are natural hormones in humans, secreted by endocrine organ(s) and poured in the circulating blood. Through blood they circulate in whole body but affect only hormone responsive organs. Theses organs carry specific proteins (receptors) on their membranes [7], cytoplasm and the nucleus [8,9] After binding to their specific receptors. the complex (receptor hormone) moves to the nucleus and bind to the hormone responsive elements (DNA) and directs to make specific protein required for the body functions. The body regulates the amount needed through intricate biochemical pathways, but when xenestrogen enter the body they increase the total amount of estrogen resulting in a phenomenon called, estrogen dominance. Xenobiotic chemicals interact with more than one estrogen receptor and can produce many biological and adverse health effects, such as early puberty in females, reduced sperm counts, altered functions of reproductive organs, obesity, altered sexspecific behaviours [10]. Parabens and phthalates are another class of compounds belonging to xenestrogen are added in daily use products thereby humans are compulsorily exposed to such compounds [11]. The current understanding of the estrogenic/ xenoestrogen actions appears to be acting via independent or dependent ER-mediated pathways. There is very scanty information available specially on parabens and phthalates however social sites are mentioning many harmful effects of these compounds. Xenestrogen are not biodegradable so, they are stored in our fat cells. Build-up of xenestrogen have been indicated in many conditions including: breast, prostate and testicular cancer, obesity, infertility, endometriosis, onset puberty, early miscarriages and diabetes. Estrogens are needed for many normal physiological functions in the human body both in woman and man. However, in woman's body it plays a major role. The organs which are affected include the brain, heart, liver, bone, adipose tissue, breast and uterus. The specific tasks of estrogens differ from tissue to tissue. For example, in the central nervous system

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estrogens protect against neurodegenerative diseases, and in adipose tissue, estrogens regulate adipogenesis, adipose deposition and adipocyte differentiation. Consequently, loss of estrogens at menopause increases a woman's developing risk of osteoporosis, neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease, and cardiovascular diseases. Menopause also is associated with weight gain [3,12,13]. In addition regulating the menstrual to cycle, estrogen affects reproduction in men and women, The reproductive tract, the urinary tract, the heart and blood vessels, blood clotting, bones growth, breasts, skin, hair, mucous membranes, pelvic muscles, and the brain. We have shown for the first time that eyes sight is also regulated by estrogens [14].

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