

## Introduction

### Estrogen in Our Bodies

- Estrogens are signaling molecules in the endocrine system produced by the ovaries in the female body, testes in the male body and adrenal glands.
- Endogenous estrogens can also be found in brain, skin and bone cell lines.
- Estrogen promotes the development and maintenance of the reproductive system in the female body and plays an important role in male sexual function.
- There are three endogenous estrogens in the body: estrone, estradiol, and estriol with the major one being estradiol.
- Estrogen receptor is conserved across all vertebrate species [1].

## Background

- Many chemicals mimic the structure of endogenous estrogens and bind with estrogen receptor at target sites resulting in an estrogenic response [2].

### Environmental Significance

- Estrogens in the Environment
  - Food: soybeans, tofu, and sunflower seeds are high in phytoestrogens [3].
  - Agricultural products: dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs) [2].
- Consumer Products
  - Bisphenol A (BPA) is in plastic lined food and beverage products such as water bottles [4].
  - Parabens are in personal care products such as shampoo, conditioner and lotions [3].
  - Birth control pills contain 17 $\alpha$ -ethinylestradiol (EE2), a synthetic estrogen that is also found in the aquatic environment at approximately 5 ng/L [5].

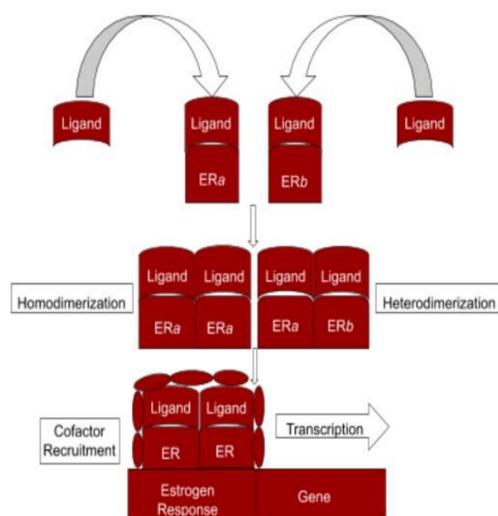


Figure 1. Estrogen receptor dynamics.

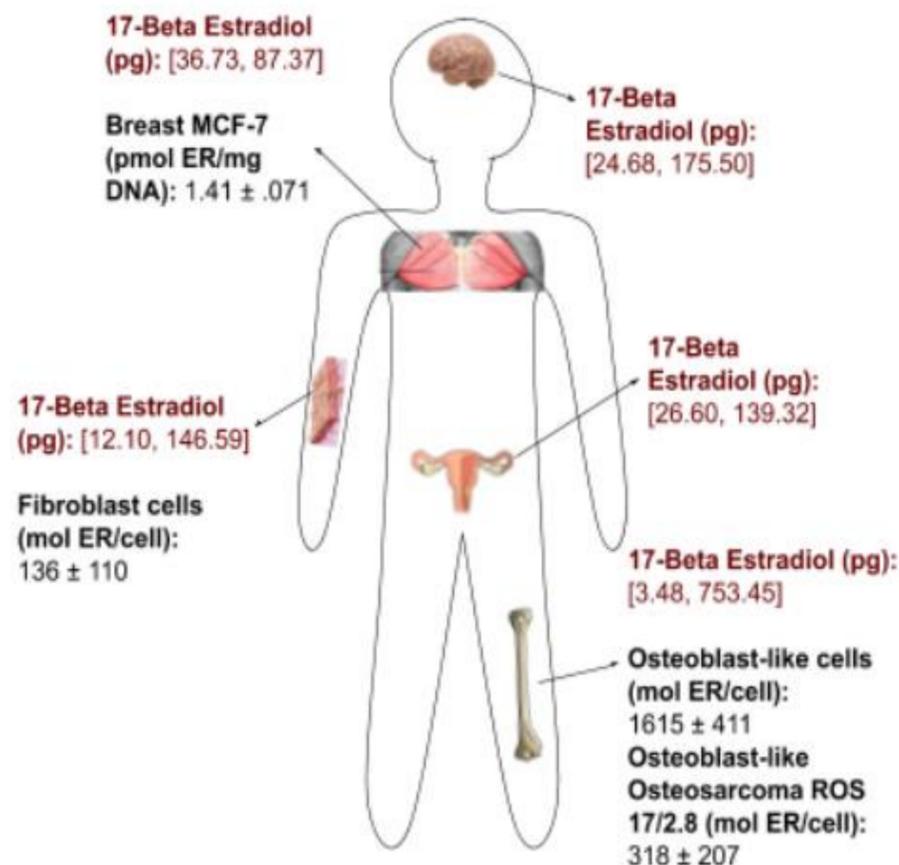


Figure 2. Body diagram representing endogenous concentrations of 17-Beta Estradiol and estrogen receptor in different cell lines. Estradiol concentrations [6]. MCF-7 estrogen receptor concentration [9]. Fibroblast and osteoblast-like estrogen receptor concentrations [10]. Osteoblast-like Osteosarcoma ROS 17/2.8 [11].

## Methods

- Uncovering endogenous concentrations of estrogen and estrogen receptors required studies from multiple sources.
- To gather the literature, a search was done across multiple databases including Scopus, PubMed, and Google Scholar
- Search terms included endogenous, estrogen, estrogen receptor, estradiol concentration, and multiple different cell lines.
- The majority of papers were studies done with estrogen that does not account for concentrations of estradiol and estrogen receptor.
- Initial search focused on TE-85 human bone osteoblast-like cells, MCF-7 human breast epithelial cells, U87 human glial brain cells, OV-90 human ovary cells, or similar cells.
- A simple spreadsheet format was utilized to organize the papers.

## Results/ Discussion

**Table 1. A:** Estradiol concentrations in brain, **B:** Estradiol concentrations in breast, **C:** Estradiol concentrations in skin, **D:** Estradiol concentrations in ovary, **E:** Estradiol concentrations in bone.

Tissue: Skin	Estradiol Concentration (pg)
MDA-MB-435	14.24
SK-MEL-28	146.59
UACC-257	130.70
LOX IMVI	12.10
UACC-62	98.71
SK-MEL-2	50.93
SK-MEL-5	72.02
MALME-3M	94.27
M14	13.95

Tissue: Glioblastoma	Estradiol Concentration (pg)
SF-295	41.51
SF-539	175.50
SF-268	24.68
U251	41.06
SNB-19	29.34
SNB-75	94.94

Tissue: Breast	Estradiol Concentration (pg)
T-47D	87.37
Hs-578T	74.11
BT-549	58.97
MDA-MB-231	36.73
MCF-7	80.75

Tissue: Ovarian	Estradiol Concentration (pg)
OVCAR-3	26.60
OVCAR-5	107.47
IGR-OV1	29.72
NCI/ADR-RES	75.10
SK-OV-3	132.33
OVCAR-8	38.83
OVCAR-4	139.32

Tissue: Bone Marrow	Estradiol Concentration (pg)
HL-60	36.61
CCRF-CEM	3.48
K562	13.88
MOLT-4	7.77
RMPI-8226	753.45
SR	26.39

- Most papers were studies done with estrogen that did not report concentrations of estradiol and estrogen receptor.
- Only about five papers were found to contain useful information pertaining to this study
  - Two papers for bone [10, 11]
  - One paper for skin [10]
  - One paper for breast [9]
  - One paper for all estradiol concentrations [6]
- The results demonstrated that there is a significant gap in scientific research when pertaining to endogenous estrogen receptor concentrations in various cell lines. The majority of literature focuses on the reproductive parts of the body such as breast and ovary cell lines.
- Papers that did include data on estrogen had concepts such as cell proliferation rather than endogenous concentrations.
- It is important to keep in mind the significance of knowing endogenous estrogen and estrogen receptor concentrations in various parts of the body. This ensures future possibilities to cancer drugs that target estrogen receptors.

## References

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### Human Health and Medical Significance

- The hope is to use the discovery of endogenous estrogens and estrogen receptors in different cell lines to develop new methods of cancer treatment.
- Endocrine therapy targeting estrogen biosynthesis and estrogen related signaling pathways [6].
  - ERa enhances cell proliferation and ERb inhibits it. One treatment for breast cancer is to block estrogen regulated tumor growth due to the high concentration of Era.
  - New medicines enhance or suppress gene activation in ERa or ERb in specific target tissues, rather than a focus on blocking estrogen [7].

### Chemical Toxicity Testing

- Chemical testing is moving towards an in-vitro assay approach, using human cell lines, rather than an animal-based approach.
- The high cost and time of animal testing results in many research gaps and an accumulation of untested chemicals.
- Increasing pressure by society to reduce animal testing due to ethical issues [8].
- Mathematical models use data from in-vitro tests to predict adverse outcome pathways in organisms.