Estrogen metabolism and nutritional influences

Estrogen is the primary hormone responsible for sexual and reproductive development in women. Once puberty begins, the body uses estrogen to regulate the first half of the menstrual cycle and then metabolizes the hormone for elimination via urination and defecation. Dietary and lifestyle modifications that support a healthy weight, like consuming a nutrient-dense dietary pattern (e.g., increasing intake of fiber and phytoestrogens) and being physically active, have been linked to the modulation of estrogen metabolism. In addition, many nutrients and nutritional bioactives have been studied for their influence on pathways of estrogen metabolism and detoxification, including but not limited to isoflavones, indole-3-carbinol, B vitamins, magnesium, limesone, calcium D-glucarate, and antioxidants.

**Production and conversion of estrogen**

- **Cholesterol** (mostly LDL) → Pregnenolone → Progesterone → Androstenedione → Testosterone → Estrone (E1) → Estradiol (E2)

**The body's systemic pool of estrogen**

- Lignans (found in fiber-rich foods) & isoflavones (found in legumes) help regulate production of sex hormone-binding globulin (SHBG), which assists in the regulation of free estrogens, testosterone, and dihydrotestosterone in circulation.

**Estrogen detoxification: bioactivation, conjugation, and elimination**

1. **Phase 1**
   - Hydroxylation (via CYP enzymes)
   - Examples: 4-OHE1, 2-OHE2

2. **Phase 2**
   - Conjugation/neutralization of the Phase 1 metabolite through methylation, glutathione
   - Examples: 4-MeOHE1, 2-MeOE1

3. **Excretion through bile & urine**

**Estrogens & estrogen receptor sensitivity**

- **ERα** (Cell proliferation & differentiation)
- **ERβ** (Antiproliferative, estrogenic activity, & downregulates ERα activation)
- **Phytoestrogens**
- **Calcium & D-glucarate**
- **NAC** (N-acetylcysteine)

**Estrogen detoxification in the liver:**

- Phase 1: Hydroxylation (via CYP enzymes) — Bioactivation of estrogen/steroid estrogen
- Phase 2: Methylation — Conjugation/neutralization of the Phase 1 metabolite through COMT, which produces positive 2-MeOE1/2-MeOE2 metabolites

**Liver & estrogen detoxification**

- Balancing Phase I and Phase II enzyme systems in the liver supports healthy estrogen detoxification and encourages the clearance of genotoxic 4-OHE1 metabolites through the induction of Nrf2, quinone reductase (NQO1), GSTs, and GSH.

**Nutrients that support:**
- Calcium D-glucarate & NAC
- Calcium + D-glucarate & NAC
- Phytoestrogens (plant-derived estrogens) examples include lignans, isoflavones (genistein, daidzein), and resveratrol. Vitamin B helps modulate tissue response.