Nordic Laboratories

Steroid Pathways

Find these Hormones on the DUTCH Report

Primary hormones (in CAPS) are made by organs by taking up cholesterol ★ and converting it locally to, for example, progesterone. Much less is made from circulating precursors like pregnenolone. For example, taking DHEA can create testosterone and estrogen, but far less than is made by the testes or ovaries, respectively.

★ → **Pregnenolone**
- (–) Ketoconazole[29], spironolactone[30], apigenin, polyphenols[31, 32]

17-hydroxylase →

17-OH-Pregnenolone
- (–) Licorice root[34, 35], spironolactone[37], azole antifungals[38], hyperglycemia[27], apegenin[31, 38]

17,20 Lyase →

DHEA
- (+) Spironolactone[84], dexamethasone[85], bile acid[86], St. John's Wort[84], forskolin[87]
- (–) Low cysteine[88], inflammation[88], LPS[89], ketoconazole[88], progestin[88], licorice[90]

17βHSD →

Androstenediol

Where is it made? Adrenal gland

DHEAS (Sulfate)

3βHSD ↓ (Pregnenolone → PROGESTERONE)
- **Where is it made?** Ovaries – less from adrenals

3βHSD ↓ (17-OH-Pregnenolone → 17-OH-Progesterone)
- (+) Hyperglycemia[27], hyperinsulinemia[28]

3βHSD ↓ (DHEA → Androstenedione)
- (+) PCBs[33], DHEA supplements[7], obesity[34]
- (–) Isoflavonoids/phytoestrogens[4], phthalates, organochlorines, BPA[5], ketoconazole[5], finasteride, dutasteride
- (+) Fenugreek[1], high ACTH/hyperadrenalism[2], PCOS[3]

3βHSD ↓ (Androstenediol → TESTOSTERONE)
- (–) Isoflavonoids/phytoestrogens[4], phthalates, organochlorines, BPA[5], ketoconazole[5], finasteride, dutasteride
- (+) Fenugreek[1], high ACTH/hyperadrenalism[2], PCOS[3]

PROGESTERONE

17-hydroxylase → **17-OH-Progesterone**

17,20 Lyase → **Androstenedione**

17βHSD → **TESTOSTERONE**

- **Where is it made?** Testes in men, from the ovaries and adrenal DHEA in women.
- (–) Enterolactone, apigenin, genistein, chrysin and other flavoniods[52],white button mushrooms[53], grape seed extract, red wine procyanidin dimers[55], PCOS[56], antifungal medications[57], metformin[58] glyphosate[59], aromatase inhibitors (letrozole, anastrozole)

*5α → **a- Pregnanediol**

5β → **β- Pregnanediol**

CYP21 ↓ (17-OH-Progesterone → Epi-Testosterone)

Epi-Testosterone

5β → **Etiocholanolone**

*5α → **5α-DHT**

5β → **5β-Androstanediol**

3αHSD ↓ (5α-DHT → 5α-Androstanediol)
- (+) Obesity and inflammation[46], high insulin[47], forskolin[48], quercetin, genistein (bioflavonoids)[49], white peony and licorice root[50], atrazine[51], rutin[39]

Aromatase (CYP19) → **Androsterone**

17βHSD ↔ **5α-Androstanediol**

Aromatase (CYP19) → **Estrone (E1)**

- Androsterone: Rutin[39], alcohol[41], abdominal obesity[42], bioflavonoids[43]
- 5α-Androstanediol: Licorice[4, 34, 35], apigenin[4,38], pyhtoestrogens[4, 43], atrazine[45]

CYP11b1 ↓ (17-OH-Progesterone → CORTISOL (active))
- **Where is it made?** Adrenal gland
- **More Cortisone:** EGCG[20], PCOS[8], curcumin[21], 7-keto-DHEA[19], progesterone[19], coffee[22], holy basil[23], bitter melon[24], hyperthyroidism[19, 26], high estrogens[19], glucocorticoids[19]

11β-HSD ↔ **Cortisone (inactive)**
- **More Cortisol:** Insulin resistance, obesity [6, 17], inflammation[18], glucocorticoids[19], hypothyroidism[25], licorice root[19], phthalates, organotins, alkylphenols[19], mother's diet during pregnancy[19], progesterone[19]

CORTISOL (active)

*5α → **α-THF**

5β → **THF**

5β ↓ (Cortisone → **THE**)

(+) Rutin[39], alcohol[41], abdominal obesity[42], bioflavonoids[43]

(–) Licorice[4, 34, 35], apigenin[4,38], pyhtoestrogens[4, 43], atrazine[45]

17βHSD ↔ **Estrone (E1)** ↔ **ESTRADIOL (E2)**

- **Where is it made?** Ovaries – lesser amounts elsewhere from DHEA/ Testosterone.
- (+) St. John's Wort[74], pesticides[75], caffeine[62], smoking[62], PAHs[74], moderate alcohol consumption[68], obesity[68]
- (–) Grapefruit[60], resveratrol[60], rosemary[65], wild yam[77], peppermint oil[78], azole antifungals[79]

CYP-3A4* → **16-OHE 1**

3A4* → **Estriol (E3)**

17βHSD ↔ (16-OHE 1 ↔ Estriol (E3))
- (–) Flavonoids[73], resveratrol[71]
- (+) Inflammation[70], smoking[71], PAHs[69]

CYP-1B1 → **4-OHE1**

COMT → **4-MeOE1**
- (–) Cruciferous vegetables[60], DIM/IC3[61], caffeine[62], soy[63], fish oil[64], rosemary extract[65], thyroxine[66,] flaxseed[67]
- (+) Estradiol[80], phthalate esters[81], rhodiola rosea, quercetin, catechin and epicatechin[83]

CYP-1A1 → **2-OHE1**

COMT → **2-MeOE1**
- (–) High sugar diet[67], moderate alcohol consumption[68], resveratrol and pterostilbene[69]
- (+) SAM-e, magnesium, B6, B12, folate, betaine (cofactors)

*CYP3A4

Many common medications induce CYP3A4, including but not limited to, phenobarbitol, phenytoin, rifampicin, and glucocorticoids.

Common medications interfere with or competitively inhibit CYP3A4 including cimetidine, tamoxifen, quinolones, fluoxetine, etc...

*5α-Reductase/5β-Reductase

5α-Reductase is best known because it makes androgens like testosterone more potent. It is also responsible for metabolizing progesterone and cortisol. If up-regulated, it may cause high androgen symptoms in men (thinning hair, prostate) and women (as in PCOS, thinning hair, acne, facial hair growth). 5β-Metabolites are less androgenic (weaker).

5α-Reductase is increased in particular by: Insulin resistance and obesity[6], DHEA supplementation[7], PCOS[8]

5α-Reductase may be decreased by: Saw palmetto and beta-sitosterol[9], reishi[10], nettle root[11], Pygeum africanum[12], PUFA and EGCG[13]

5β-Reductase may be affected by some of the above listed things as well (often to a lesser degree).

5β-Reductase may be increased by: Insulin resistance, high triglycerides[14], PCOS[15]

5β-Reductase may be decreased by: Licorice[16]

Cortisol Metabolism/Clearance

Cortisol is metabolized by 5α/5β-reductase (and 3α-HSD) to α/β-THF & THE for excretion. This process is particularly increased in obesity, high insulin and hyperthyroid. It may be slowed in cases of hypothyroidism, anorexia or poor liver function.

The information on this chart is for educational purposes only and is not a suggestion for supplementation with any of the listed items. Please see the DUTCH Test Treatment Guide for other factors affecting the production of primary reproductive and adrenal hormones.

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