5-Alpha Reductase
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Metabolism
5-alpha-reductase (5AR) is the enzyme that converts:
- Testosterone into 5-alpha-dihydrotestosterone (DHT)
- Androstenedione into andosterone
- Cortisol into allo-tetrahydrocortisol

Two ratios are commonly used to assess 5-alpha-reductase activity:
- Andosterone : Etiocolanone
- Allo-tetrahydrocortisol : tetrahydrocortisol

Increased
Elevated 5-alpha-reductase activity is associated with polycystic ovary syndrome and hirsutism in women; benign prostatic hypertrophy and premature baldness in men; and obesity and insulin resistance in both genders. (Vassiliadi, Barber et al. 2009)

Obesity and insulin resistance are related with elevated 5-alpha-reductase activity. (Tomlinson, Finney et al. 2008)

Decreased
Over-inhibition of 5-alpha reductase results in decreased production of dihydrotestosterone (DHT) and increased levels of testosterone. The resulting conversion of testosterone estradiol may cause gynecomastia, which is a side effect of 5-alpha reductase inhibitor drugs.

Over-inhibition or 5-alpha reductase also results in decreased amounts of the metabolites of DHT, which include 3beta-Adiol (5alpha-androstane-3beta,17beta-diol), an anti-proliferative hormone that may help prevent prostate cancer. (Dondi, Piccolella et al. 2010)

Congenital 5-alpha-reductase deficiency results in male pseudohermaphroditism. (al-Attia 1997)
(Hochberg, Chayen et al. 1996)

Conventional Treatments
Finasteride and Dutasteride
5-Alpha-reductase inhibitor drugs are used in benign prostatic hyperplasia, prostate cancer, and baldness (androgenic alopecia). They include finasteride (Proscar, Propecia) and dutasteride (Avodart).
Adverse drug reactions (ADRs) to 5-alpha reductase inhibitors are dose dependant. Common ADRs include impotence, decreased libido, and decreased ejaculate volume. Rare ADRs include breast tenderness and enlargement, and allergic reaction.

**Progesterone and DHEA**

DHEA up-regulates 5AR activity. (Stomati, Monteleone et al. 2000)

Progesterone inhibits 5-alpha reductase (Cassidenti, Paulson et al. 1991)

**Natural Therapies**

5-alpha reductase inhibitors include zinc, GLA and EPA, Saw palmetto, Vitamin D3, Green tea, Ganoderma lucidum and astaxanthin.

**Zinc and Vitamin B6**

A study showed that the livers of zinc-deficient rats exhibited a higher aromatization of testosterone to estradiol than did those of both groups of controls. (Om and Chung 1996)

When added at concentrations of 3 or 9 mmol/l, zinc was a potent inhibitor of 5 alpha-reductase activity in human skin. Vitamin B6 potentiated the inhibitory effect of zinc. (Stamatiadis, Bulteau-Portois et al. 1988)

**GLA and EPA**

The essential fatty acids gamma-linolenic and eicosapentaenoic acids (GLA and EPA) have been shown to inhibit 5AR. (Pham and Ziboh 2002)

**Saw palmetto**

Lauric acid, oleic acid, myristic acid, and linoleic acid, major constituents of Saw palmetto (Serenoa repens) extract, exerted binding activities of alpha(1)-adrenergic, muscarinic and 1,4-DHP receptors and inhibited 5alpha-reductase activity. (Abe, Ito et al. 2009) (Abe, Ito et al. 2009) (Habib, Ross et al. 2005) (Raynaud, Cousse et al. 2002) (Bayne, Donnelly et al. 1999)

**Isoflavonoids and Lignans**

In genital skin fibroblasts, genistein, biochanin A and equol were the most potent inhibitors of 5 alpha-reductase activity, each resulting in greater than 80% inhibition at a concentration of 100 microM. The IC50 values for genistein and a seven-compound mixture were approximately 35 microM and 20 microM (2.9 microM of each compound) respectively. Of the lignans, enterolactone was the most potent inhibitor. Inhibition by biochanin A was shown to be reversible. When genital skin fibroblast homogenates were used, biochanin A was found to inhibit 5 alpha-reductase isozymes 1 and 2 to differing extents (30% and 75% respectively). Genistein was shown to inhibit 5 alpha-reductase 2 in a non-competitive nature (Vmax and Km values without and with inhibitor were 30 and 20 pmol/mg protein per h and 177 and 170 nM respectively). (Evans, Griffiths et al. 1995)
**Ganoderma lucidum**

Ganoderic acid DM, with 5alpha-reductase inhibitory and androgen receptor (AR) binding activity, isolated from the ethanol extracts of Ganoderma lucidum, can inhibit prostate cancer cell growth and block osteoclastogenesis. (Liu, Shiono et al. 2009)


**Green Tea**

ECGC and kaempferol from green tea have been shown to inhibit 5-alpha reductase activity. (Park, Yeom et al. 2006) (Hiipakka, Zhang et al. 2002) (Liao and Hiipakka 1995)

**Astaxanthin**

Astaxanthin, a carotenoid, demonstrated 98% inhibition of 5alpha-reductase at 300 microg/mL in vitro. (Anderson 2005)
References


