5alpha-androstane-3beta,17beta-diol (3-beta Adiol)

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5alpha-androstane-3beta,17beta-diol is referred to as 3beta-diol, 3beta-Adiol or 3betaAdiol.

The nomenclature can be confusing as there are several androstane molecules with differences in alpha and beta (in three places) and 3 and 5 (in 2 places).

Deficiency
Decreased 3-beta Adiol can result from decreased activity of 5-alpha reductase, which also lowers 5-alpha DHT.

Metabolism

Figure 1: DHEA.jpg

Estrogen Receptors
Estrogen effects are mediated through two different estrogen receptors: alpha and beta (ER-alpha and ER-beta).

3beta-Adiol is a more efficient activator of estrogen receptor beta than 7alpha-hydroxy-dehydroepiandrosterone (DHEA, a CYP7B1 product). (Pettersson, Holmberg et al. 2008)

Prostate Cancer
In the prostate, ER-beta is highly expressed in the epithelial compartment, where it is the prevailing isoform.

ER-beta is an anti-proliferative receptor, 3betaAdiol is an ER-beta ligand, and CYP7B1 is the enzyme that regulates ER-beta function by regulating the level of 3betaAdiol. (Weihua, Lathe et al. 2002)

5alpha-androstane-3beta,17beta-diol (3beta-Adiol) inhibits the migration of prostate cancer cell lines via ER-beta activation. (Dondi, Piccolella et al. 2010)

5alpha-androstane-3beta,17beta-diol binds to ER-beta, but not to androgen receptors. (Oliveira, Coelho et al. 2007)

5alpha-androstane-3beta,17beta-diol inhibits prostate cancer cell migration through activation of estrogen receptor beta. (Guerini, Sau et al. 2005)

Breast Cancer

Estrogen receptor-alpha promotes breast cell proliferation, while ER-beta inhibits proliferation and prevents breast cancer development via G2 cell cycle arrest. (Paruthiyil, Parmar et al. 2004)

The androgen metabolite 5alpha-androstane-3beta,17beta-diol (3betaAdiol) induces breast cancer growth via estrogen receptor-alpha. (Sikora, Cordero et al. 2009)

Stress

Arginine-vasopressin (AVP) and corticotrophin-releasing hormone (CRH) are two major regulatory peptides in the brain involved in stress regulation.

3beta-diol regulates arginine vasopressin, mediated by estrogen receptor-beta, in pre- and post-pubertal male rats. (Pak, Chung et al. 2009)

Estrogen receptor-beta mediates dihydrotestosterone-induced stimulation of the arginine vasopressin promoter in neuronal cells. (Pak, Chung et al. 2007)

5alpha-androstane-3beta, 17beta-diol has an estrogenic effect on the behavioral response to stress and on CRH regulation. (Huang, Zhu et al. 2008)

Studies using both in vitro and in vivo approaches provide compelling evidence that 3beta-Diol is an important modulator of the stress response mediated by the hypothalamo-pituitary-adrenal axis. Furthermore, the actions of 3beta-Diol are mediated by estrogen receptors, and not androgen receptors, often through a canonical estrogen response element in the promoter of a given target gene. (Handa, Pak et al. 2008)

The androgen 5alpha-dihydrotestosterone and its metabolite 5alpha-androstan-3beta, 17beta-diol inhibit the hypothalamo-pituitary-adrenal response to stress by acting through estrogen receptor beta-expressing neurons in the hypothalamus. (Lund, Hinds et al. 2006)
Miscellaneous

The androgen derivative 5alpha-androstane-3beta,17beta-diol inhibits tumor necrosis factor alpha and lipopolysaccharide induced inflammatory response in human endothelial cells and in mice aorta. (Norata, Cattaneo et al. 2010)

Cobalt protoporphyrin administered subcutaneously to adult male rats caused a marked reduction in the conversion of 5 alpha-androstane-3 beta-17 beta-diol (3 beta-adiol) to its main triol derivative (6 alpha-atriol) by homogenates of the pituitary but not of the prostate or brain (ventromedial hypothalamus and cortex). (Jellinck and Galbraith 1991)


The androgen metabolite, 5alpha-androstane-3beta, 17beta-diol, is a potent modulator of estrogen receptor-beta1-mediated gene transcription in neuronal cells. (Pak, Chung et al. 2005)

Alcohol

Ethanol directly increases dihydrotestosterone conversion primarily to 5α-androstan-3β, 17β-diol in rat Leydig cells. (Murono and Fisher-Simpson 1985)


Norata, G. D., P. Cattaneo, et al. (2010). "The androgen derivative 5alpha-androstane-3beta,17beta-diol inhibits tumor necrosis factor alpha and


