ADVERSE REACTIONS

No reports.

INTERACTIONS

DRUGS

None known.

NUTRITIONAL SUPPLEMENTS

None known.

HERBS

None known.

OVERDOSAGE

There are no reports of overdosage.

DOSAGE AND ADMINISTRATION

The optimal dosage of 8-PN for any health condition is unknown.

A number of 8-PN-containing dietary supplements are available which are marketed for breast enhancement. Because of the lack of long-term safety studies, these supplements are not recommended for use.

Beer is the major dietary source of 8-PN. The concentration of 8-PN in most beers is below 30 micrograms per liter. Some beers, particularly strong ales, have been reported to contain concentrations of up to 250 micrograms (0.24 milligrams) or higher per liter. Beer itself contains isoxanthohumol, a mild phytoestrogen which can be metabolized to 8-PN via the intestinal microflora. This could increase the exposure to 8-PN from beer by up to 4 mg per liter.

LITERATURE

Böttner M, Christoffel J, Wuttke W. Effects of long-term treatment with 8-PN and oral estradiol on the GH-IGF-1 axis and lipid metabolism in rats. *J Endocrinol.* 2008;198:395-401.

Bowe J, Li XF, Kinsey-Jones J, et al. The hop phytoestrogen, 8-PN, reverses the ovariectomy-induced rise in skin temperature in an animal model of menopausal hot flushes. *J Endocrinol.* 2006;191(2):399-405.

Brunelli E, Minassi A, Appendino G, et al. 8-PN, inhibits estrogen receptor-alpha mediated cell growth and induces apoptosis in MCF-7 breast cancer cells. *J Steroid Biochem Mol Biol.* 2007;107(3-5):140-148.

Christoffel J, Rimoldi G, Wuttke W. Effects of 8-PN on the hypothalamo-pituitary-uterine axis in rats after 3-month treatment. *J Endocrinol.* 2006;188(3):397-405.

Delmulle L, Berghe TV, Keukeleire DD, et al. Treatment of PC-3 and DU145 prostate cancer cells by prenylflavonoids from hop (Humulus lupulus L.) induces a caspase-independent form of cell death. *Phytother Res.* 2008;22(2):197-203.

Diel P, Thomae RB, Caldarelli A, et al. Regulation of gene expression by 8-PN in uterus and liver of Wistar rats. *Planta Med.* 2004;70(1):39-44.

Milligan S, Kalita J, Pocock V, et al. Oestrogenic activity of the hop phyto-oestrogen, 8-PN. *Reproduction.* 2002;123(2):235-242.

Milligan SR, Kalita JC, Pocock V, et al. The endocrine activities of 8-PN and related hop (*Humulus lupulus* L.) flavonoids. *J Clin Endocrinol Metab.* 2000;85(12):4912-4915.

Nikolic D, Li Y, Chadwick LR, et al. In vitro studies of intestinal permeability and hepatic and intestinal metabolism of 8-PN, a potent phytoestrogen from hops (Humulus lupulus L.). *Pharm Res.* 2006;23(5):864-872.

Nikolic D, Li Y, Chadwick LR, et al. Metabolism of 8-PN, a potent phytoestrogen from hops (Humulus lupulus), by human liver microsomes. *Drug Metab Dispos.* 2004;32(2):272-279.

Pepper MS, Hazel SJ, Hümpel M, et al. 8-PN, a novel phytoestrogen, inhibits angiogenesis in vitro and in vivo. *J Cell Physiol.* 2004;199(1):98-107.

Rad M, Hümpel M, Schaefer O, et al. Pharmacokinetics and systemic endocrine effects of the phyto-oestrogen 8-PN after single oral doses to postmenopausal women. *Br J Clin Pharmacol.* 2006;62(3):288-296.

Rimoldi G, Christoffel J, Wuttke W. Morphologic changes induced by oral long-term treatment with 8-PN in the uterus, vagina, and mammary gland of castrated rats. *Menopause.* 2006;13(4):669-677.

Roelens F, Heldring N, Dhooge W, et al. Subtle side-chain modifications of the hop phytoestrogen 8-PN result in distinct agonist/antagonist activity profiles for estrogen receptors alpha and beta. *J Med Chem.* 2006;49(25):7357-7365.

Rong H, Boterberg T, Maubach J, et al. 8-PN, the phytoestrogen in hops and beer, upregulates the function of the E-cadherin/catenin complex in human mammary carcinoma cells. *Eur J Cell Biol.* 2001;80(9):580-585.

Schaefer O, Hümpel M, Fritzemeier KH, et al. 8-PN is a potent ERalpha selective phytoestrogen present in hops and beer. *J Steroid Biochem Mol Biol.* 2003;84(2-3):359-360.

Sehmisch S, Hammer F, Christoffel J, et al. Comparison of the phytohormones genistein, resveratrol and 8-PN as agents for preventing osteoporosis. *Planta Med.* 2008;74(8):794-801.

Zierau O, Hauswald S, Schwab P, et al. Two major metabolites of 8-PN are estrogenic in vitro. *J Steroid Biochem Mol Biol.* 2004;92(1-2):107-110.

19-Norandrostenedione

It is illegal to use or possess 19-Norandrostenedione except if enrolled in FDA-allowed clinical trials or if prescribed by a qualified physician.

DESCRIPTION

Following the passage of the Dietary Supplement Health and Education Act (DSHEA) of 1994, a number of putative anabolic substances, including 19-norandrostenedione, began to be marketed as dietary supplements. In March 2004, Senators Joseph Biden and Orrin Hatch co-authored and introduced a bill known as the Anabolic Steroid Control Act of 2004. The Act revised the term "anabolic steroid" to mean any drug or hormonal substance chemically and pharmacologically related to testosterone (other than estrogens, progestins, corticosteroids, and dehydroepiandrosterone [DHEA]). The list attached to the bill contained 59 specific substances, 26 of which were added to the existing 1990 list of steroids that are classified as schedule III controlled substances. The two isomers of 19-norandrostenedione—19-nor-4-androstene-3, 17-dione and 19-nor-5-androstene-3, 17-dione—were included in the list. The bill passed the Senate by unanimous consent on October 6, 2004, passed the House of Representatives two days later and was signed by President George W. Bush on October 22, 2004. It went into effect on January 20, 2005.

19-norandrostenedione refers to two steroid isomers that had been marketed as dietary supplements and mainly used by body builders. The difference between the two 19-norandrostenedione isomers is in the position of the double bond in the cyclopentanoperhydrophenanthrene ring structure. The delta4 isomer has a double bond between carbons 4 and 5; the delta5 isomer has a double bond between carbons 5 and 6.

The delta4 isomer is also known as 19-nor-4-androstene-3, 17-dione. The delta5 isomer is also known as 19-nor-5-androstene-3, 17-dione. The delta4 isomer is sometimes referred to as 19-nor and is the more popular of the two substances. The term "nor" refers to the absence of a 19 methyl group on the steroid ring structure. 19-norandrostenedione is synthesized in the adrenal gland and gonads from androstenedione. It is metabolized by the aromatase complex to estrone. The delta4, as well as delta5, 19-norandrostenedione may also be metabolized by the enzyme 17 beta-hydroxy steroid dehydrogenase to 19-nortestosterone, also known as nandrolone. In this monograph, 19-norandrostenedione will generally be used in the singular to refer to both the delta4 and delta5 isomers.

ACTIONS AND PHARMACOLOGY

ACTIONS

Supplemental 19-norandrostenedione is a putative anabolic substance.

MECHANISM OF ACTION

19-norandrostenedione may be metabolized to 19-nortestosterone in both men and women. 19-Norandrostenedione, also known as nandrolone, is the basic substance of some very popular injectable anabolic steroids. 19-Norandrostenedione is not metabolized to testosterone. Whether increases in 19-nortestosterone levels that may be produced by taking oral 19-norandrostenedione would be sustained long enough to show increase in nitrogen retention and muscle strength and mass is unknown.

PHARMACOKINETICS

There is scant human pharmacokinetic data on 19-norandrostenedione. Absorption appears variable, but some absorption does occur. Following ingestion of 19-norandrostenedione, metabolites, including 19-norandrosterone and 19-noretiocholanolone, appear in the urine. 19-norandrostenedione and 19-noretiocholanolone are detectable in the urine for seven to 10 days after a single 50-mg oral dose. Specific metabolites of 19-nor-5-androstene-3, 17-dione are 19-nor-dehydroandrosterone and 19-nordehydroepiandrosterone. In the later stages of excretion, higher levels of 19-noretiocholanolone relative to 19-norandrosterone indicate intake of 19-nor delta5 steroids.

INDICATIONS AND USAGE

The claim that supplemental 19-norandrostenedione has anabolic effects is unsubstantiated. The use of this substance may pose serious health risks in some.

RESEARCH SUMMARY

There is no research showing that either oral or injectable 19-norandrostenedione has significant anabolic effects.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

19-norandrostenedione is contraindicated in those with prostate, breast, ovarian and uterine cancer and those at risk for these cancers. 19-norandrostenedione is also contraindicated in those who are hypersensitive to any component of a 19-norandrostenedione-containing preparation.

PRECAUTIONS

19-norandrostenedione is illegal to use or possess except if enrolled in an FDA-allowed clinical trial or if prescribed by a qualified physician.

ADVERSE REACTIONS

No data are available on the long-term safety of taking supplemental 19-norandrostenedione. Adverse effects of exogenous testosterone in men include acne, testicular atrophy, gynecomastia, behavioral changes and possibly an increased risk of prostate cancer. Adverse effects of exogenous testosterone in women include hirsutism, deepening of the voice, acne, clitoral hypertrophy, amenorrhea, male-pattern baldness and coarsening of the skin. In adolescents, exogenous testosterone can lead to early closing of bone growth plates and decreased adult height. Other adverse effects of testosterone include hepatic failure and increased platelet aggregation.

Many, if not all, of the above adverse reactions may occur with long-term use of 19-norandrostenedione.

INTERACTIONS

No drug, nutritional supplement, food or herb interactions have yet been reported.

OVERDOSAGE

No reports of overdosage.

DOSAGE AND ADMINISTRATION

19-norandrostenedione is illegal to use or possess except if enrolled in an FDA-allowed clinical trial or if prescribed by a qualified physician.

LITERATURE

Anabolic Steroid Control Act of 2004. http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108_cong_public_laws&docid=f:publ358.108.pdf. Accessed September 22, 2008.

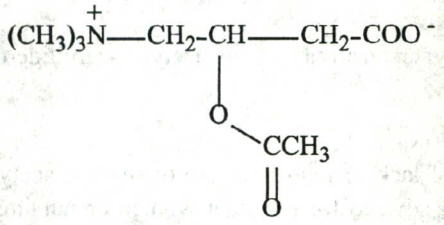
Uralets VP, Gillette PA. Over-the-counter anabolic steroids 4-androsten-3, 17-dione; 4-androsten-3beta, 17beta-diol; and 19-nor-4-androstene-3, 17-dione: excretion studies in men. *J Anal Toxicol.* 1999;23:357-366.

Uralets VP, Gillette PA. Over-the-counter delta5 anabolic steroids 5-androsten-3, 17-dione, 5-androsten-3beta, 17 beta-diol; dehydroxyepiandrosterone; and 19-nor-5-androstene-3, 17-dione: excretion studies in men. *J Anal Toxicol.* 2000;24:188-193.

Acetyl-L-Carnitine

DESCRIPTION

Acetyl-L-Carnitine is the acetyl ester of L-carnitine. It occurs naturally in animal products. Chemically, acetyl-L-carnitine is known as beta-acetoxy-gamma-N, N, N-trimethylamino-butyrate and is represented by the following chemical structure:



Acetyl-L-Carnitine

Acetyl-L-carnitine is also known as acetyl-carnitine, L-acetycarnitine, acetylcarnitine, acetyl levocarnitine, N-acetyl-L-carnitine, ALC and ALCAR.

Acetyl-L-carnitine is a delivery form for both L-carnitine and acetyl groups.

ACTIONS AND PHARMACOLOGY

ACTIONS

Supplemental acetyl-L-carnitine may have neuroprotective activity. In addition, it, like L-carnitine, may have cardioprotective activity and may beneficially affect cardiac function. It may enhance sperm motility. Acetyl-L-carnitine may also have cytoprotective, antioxidant and anti-apoptotic activity.

MECHANISM OF ACTION

Acetyl-L-carnitine is a delivery form for L-carnitine and acetyl groups. The functions of L-carnitine include transport of long-chain fatty acids across the mitochondrial membranes into the mitochondria (wherein their metabolism produces bioenergy) and transport of small-chain and medium-chain fatty acids out of the mitochondria in order to, among other things, maintain normal coenzyme A levels in these organelles. It may also have antioxidant activity.

The acetyl component of acetyl-L-carnitine provides for the formation of the neurotransmitter acetylcholine. Abnormal acetylcholine metabolism in the brain, leading to acetylcholine deficits in certain brain regions, is thought to be associated with age-related dementias, including Alzheimer's disease.

Acetyl-L-carnitine has been found to decrease glycation of lens proteins *in vitro.* It is thought to do so by acetylating certain lens proteins called crystallins. In so doing it protects them from glycation-mediated damage.

Many biochemical changes occur during the aging process. These include decreased cardiolipin synthesis in the heart and impaired mitochondrial function. Cardiolipin is a key phospholipid necessary for mitochondrial transport processes in the heart. Mitochondria are vital for the production of cellular energy. Experiments in aged rats have shown that acetyl-L-carnitine supplementation leads to improved mitochondrial function and increased cardiolipin production.

Acetyl-L-carnitine serves as a readily accessible energy pool for use in both activation of respiration and motility in human spermatozoa.

PHARMACOKINETICS

The pharmacokinetics of acetyl-L-carnitine is similar to L-Carnitine (see L-carnitine). There is speculation that it is better absorbed than L-carnitine, but this has not yet been established.

INDICATIONS AND USAGE

Acetyl-L-carnitine has recently demonstrated some efficacy as a possible neuroprotective agent and may be indicated for use in strokes, Alzheimer's disease, Down's syndrome and for the management of various neuropathies. It may also have anti-aging properties. Research regarding acetyl-L-carnitine's possible beneficial effect on sperm motility is