

Those who develop gastrointestinal symptoms (flatus, bloating, diarrhea) with the use of dietary fiber should exercise some degree of caution in the use of prebiotics. Those receiving whole body radiation or radiation to the gastrointestinal tract should avoid prebiotic supplements.

Pregnant women and nursing mothers should only use prebiotic supplements if prescribed by their physicians.

ADVERSE REACTIONS

Doses of prebiotic oligosaccharides up to 10 grams daily are well tolerated. Higher doses may cause gastrointestinal symptoms, such as flatulence, bloating and diarrhea.

INTERACTIONS

NUTRITIONAL SUPPLEMENTS

Alpha-galactosidase: Concomitant use of alpha-galactosidase (see Supplemental Enzymes) and soy oligosaccharides may decrease the effectiveness of the soy oligosaccharides.

Minerals (calcium, magnesium): Concomitant intake of calcium or magnesium and prebiotics may enhance the colonic absorption of these minerals.

Probiotics: Concomitant intake of probiotics and prebiotics may enhance the possible effectiveness of both the probiotics and the prebiotics.

FOODS

Prebiotic oligosaccharides may enhance the colonic absorption of calcium and magnesium in foods.

DOSAGE AND ADMINISTRATION

Fructo-oligosaccharides, (FOS) and inulins are available in nutritional supplements and in functional foods. Dosage is variable for both FOS and inulins and ranges from 4 to 10 grams. Those who use more than 10 grams daily of FOS or inulins should split the dosage throughout the day. Doses higher than 30 grams daily of FOS or inulins may cause significant gastrointestinal discomfort (flatulence, bloating, cramping, diarrhea).

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For additional Literature, see Fructo-Oligosaccharides, Inulins, Lactulose, Transgalacto-Oligosaccharides.

Pregnenolone

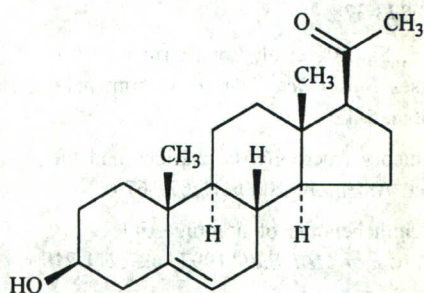
DESCRIPTION

Pregnenolone is a steroid naturally found in animal tissues, especially in the gonads, adrenal gland and brain. Pregnenolone is synthesized from cholesterol and is a precursor for the biosynthesis of steroid hormones. In the adrenal gland, pregnenolone is a precursor to the mineralocorticoid aldosterone, the glucocorticoid cortisol, as well as dehydroepiandrosterone (DHEA) and progesterone. In the ovary, pregnenolone is a precursor to estrogens and progesterone, and, in the testis, pregnenolone is a precursor to testosterone.

Pregnenolone and its metabolite pregnenolone sulfate are now known to be synthesized in the brain either *de novo* from cholesterol or from other metabolites. Pregnenolone and pregnenolone sulfate found in the brain and central nervous system are referred to as neurosteroids.

Pregnenolone is known chemically as 3-Hydroxypregn-5-en-20-one; delta 5-pregnen-3 beta-ol-20-one, and 17 beta-(1-

ketoethyl)-delta 5-androstene-3 beta-ol. Its abbreviation is PREG and the abbreviation of its metabolite, progesterone sulfate, is PREG S. Pregnenolone is a lipophilic solid substance that is sparingly soluble in water. Pregnenolone has the following chemical structure:



Pregnenolone

ACTIONS AND PHARMACOLOGY

ACTIONS

Supplemental pregnenolone has putative memory-enhancing activity.

MECHANISM OF ACTION

Memory enhancement has been observed in aged animals when given pregnenolone or pregnenolone sulfate. Pregnenolone sulfate is both a gamma-aminobutyrate (GABA) antagonist and a positive allosteric modulator at the N-methyl-D-aspartate (NMDA) receptor and may reinforce neurotransmitter systems that may decline with age.

Pregnenolone sulfate was found to stimulate acetylcholine release in the adult rat hippocampus. Acetylcholine release may be due to pregnenolone sulfate's negative modulation of the GABA (A) receptor complex and positive modulation of the NMDA receptor. While a modest increase in acetylcholine release facilitates memory processes, elevation of acetylcholine beyond an optimal level is ineffective in doing so.

PHARMACOKINETICS

Little is known about the pharmacokinetics (PK) of pregnenolone in humans. Some PK studies have been done in animals. The absorption of pregnenolone, similar to the absorption of most steroids, is variable. It appears that some pregnenolone is absorbed from the small intestine and distributed throughout the body. How much is taken up by the liver and metabolized is unclear. Likewise, it is unclear how much of an ingested pregnenolone dose is taken up by the brain. Metabolites of injected pregnenolone in the rat brain include pregnenolone sulfate, progesterone, 5 alpha-pregnane-3, 20-dione, 3 alpha-hydroxy-5 alpha-pregnan-20-one or allopregnanolone and DHEA. In other tissues, pregnenolone may be metabolized to DHEA, testosterone, estrogens, cortisol and aldosterone.

INDICATIONS AND USAGE

Pregnenolone may have some efficacy as a memory enhancer; this has so far been demonstrated in various animal models but not yet in humans. There are unsubstantiated claims that pregnenolone is useful in Alzheimer's disease, some forms of cancer and arthritis, in degenerative diseases associated with aging in general and in obesity.

RESEARCH SUMMARY

There are several studies showing a correlation between deficiencies in cognitive performance in aged animals and low pregnenolone levels in the brains of these animals, especially in the hippocampus. Performance on memory tests have been shown to improve in these animals when hippocampal pregnenolone levels were increased via intraperitoneal or bilateral intrahippocampal injection of pregnenolone sulfate.

There is direct evidence from many of these studies that pregnenolone sulfate stimulates release of acetylcholine in the hippocampus. There is additional evidence that suggests that exogenous pregnenolone can reinforce neurotransmitter systems that normally decline with age. A "global stimulatory effect on central cholinergic neurotransmission" has been suggested by one research group.

Though significant favorable results have been obtained with respect to memory enhancement in aged animals, human studies have yet to commence. These are warranted. Meanwhile, claims that supplemental pregnenolone is helpful in Alzheimer's disease are unsubstantiated. And there is no credible evidence that pregnenolone is useful in the treatment of arthritis, cancer, degenerative diseases or obesity.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Pregnenolone is contraindicated in those with prostate, breast and uterine cancer. Known hypersensitivity to a pregnenolone-containing product.

PRECAUTIONS

Pregnenolone should be avoided by children, pregnant women and nursing mothers.

Because of the theoretical possibility that pregnenolone may lower seizure threshold—pregnenolone sulfate negatively modulates GABA (A) receptors in animals—those with seizure disorders should avoid pregnenolone.

ADVERSE REACTIONS

To date there are no reported significant adverse effects. Mild gastrointestinal effects, such as nausea, have been noted. However, pregnenolone may be converted to steroids such as DHEA, and DHEA does cause various adverse effects such as acne and hair loss, especially in women.

INTERACTIONS

There are no reported drug, nutritional supplement, food or herb interactions to date.

OVERDOSAGE

No reported overdosage.

DOSAGE AND ADMINISTRATION

Typical pregnenolone doses are 5 to 50 milligrams daily. The safety of taking pregnenolone at any dose, especially long term, is unknown.

LITERATURE

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Probiotics

DESCRIPTION

Probiotics are defined as live microorganisms, including *Lactobacillus* species, *Bifidobacterium* species and yeasts, that may beneficially affect the host upon ingestion by improving the balance of the intestinal microflora. The dietary use of live microorganisms has a long history. Mention of cultured dairy products is found in the Bible and the sacred books of Hinduism. Soured milks and cultured dairy products, such as kefir, koumiss, leben and dahi, were

often used therapeutically before the existence of microorganisms was recognized. The use of microorganisms in food fermentation is one of the oldest methods for producing and preserving food. Much of the world depends upon various fermented foods that are staples in the diet.

Élie Metchnikoff, the father of modern immunology, spoke highly about the possible health benefits of the lactic acid bacteria (LAB) *Lactobacillus bulgaricus* and *Streptococcus thermophilus* in his writings at the turn of the last century. He wrote in his book, *The Prolongation of Life*, that consumption of live bacteria, such as *Lactobacillus bulgaricus* and *Streptococcus thermophilus*, in the form of yogurt was beneficial for gastrointestinal health, as well as for health in general, and for longevity. Some recent research suggests that certain live microorganisms may have immunomodulatory and anticarcinogenic effects, as well as other health benefits. There is presently much active research focusing on the development of target-specific probiotics containing well-characterized bacteria that are selected for their health-enhancing characteristics. These new probiotics are entering the marketplace in the form of nutritional supplements and functional foods, such as yogurt functional food products.

The gastrointestinal tract represents a complex ecosystem in which a delicate balance exists between the intestinal microflora and the host. The microflora are principally comprised of facultative anaerobes and obligate anaerobes. Approximately 95% of the intestinal bacterial population in humans is comprised of obligate anaerobes, including *Bifidobacterium*, *Clostridium*, *Eubacterium*, *Fusobacterium*, *Peptococcus*, *Peptostreptococcus* and *Bacteroides*. Approximately 1% to 10% of the intestinal population is comprised of facultative anaerobes, including *Lactobacillus*, *Escherichia coli*, *Klebsiella*, *Streptococcus*, *Staphylococcus* and *Bacillus*. Aerobic organisms are not present in the intestinal tract of healthy individuals with the exception of *Pseudomonas*, which is present in very small amounts. Most of the bacteria are present in the colon where the bacterial concentration ranges between 10^{11} to 10^{12} colony-forming units (CFU) per milliliter.

The intestinal microflora are important for maturation of the immune system, the development of normal intestinal morphology and in order to maintain a chronic and immunologically balanced inflammatory response. The microflora reinforce the barrier function of the intestinal mucosa, helping in the prevention of the attachment of pathogenic microorganisms and the entry of allergens. Some members of the microflora may contribute to the body's requirements for certain vitamins, including biotin, pantothenic acid and vitamin B₁₂. Alteration of the microbial flora