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COVER STORY

Replenish Testosterone *Naturally*

Plant extracts favorably alter hormone metabolism and improve sexual desire in men

Through a variety of mechanisms, aging men suffer from the dual effects of having too little testosterone and excess estrogen. The result is a testosterone/ estrogen imbalance that can severely inhibit sexual desire and performance. In youth, low amounts of estrogen are used to turn off the powerful cell-stimulating effects of testosterone. As estrogen levels increase with age, testosterone cell stimulation may be locked in the "off" position, thus reducing sexual arousal and sensation and causing the common loss of libido so common in aging men.

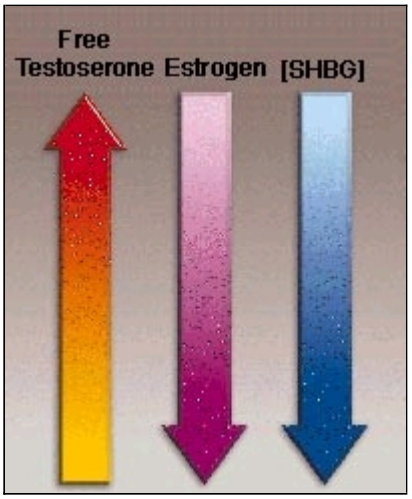
The genital/pelvic region is packed with testosterone receptors that are ultra-sensitive to free testosterone-induced sexual stimulation. Clinical studies using testosterone injections, creams or patches have not always provided a long-lasting libido enhancing effect in aging men.

We now know why. Aging men sometimes convert testosterone to estrogen. The estrogen is then taken up by testosterone receptor sites in cells throughout the body. When an estrogen molecule occupies a testosterone receptor site on a cell membrane, it blocks the ability of serum testosterone to induce a healthy hormonal signal. It does not matter how much serum free testosterone is available if excess estrogen is competing for the same cellular receptor sites.

Testosterone is a hormone responsible for sex drive in both men and women. For testosterone to promote youthful sexual interest, satisfaction and performance, it must be freely available to cell receptor sites in the brain, the nerves, muscles and genitals. As people age, testosterone becomes bound to serum globulin and is not available to the cell receptor sites were it is needed to initiate sex stimulating centers in the brain. The component in the blood that renders free testosterone inactive is called sex hormone-binding globulin (SHBG). Excess estrogen can increase the production of SHBG and block testosterone-receptor sites. This means there are two mechanisms by which excess estrogen interferes with sex dive in aging males.

For testosterone to produce long-lasting libido enhancing effects, it must be kept in the "free" form in the bloodstream. Bound testosterone is not able to be picked up by testosterone receptors on cell membranes. For aging men, it is desirable to suppress excess levels of SHBG and estrogen while boosting free testosterone to the level of a young man. There is now a natural way of modulating testosterone and estrogen levels in aging men that does not require expensive prescription drugs.

Restoring youthful hormone balance can have a significant impact on male sexuality. To reiterate, the hormone modulation objectives that most aging men need to facilitate sexual rejuvenation involves an increase in "free" testosterone coupled by a decrease in both estrogen and SHGD levels.



Increasing testosterone by suppressing excess estrogen

For many men, a safe and easy way to increase free testosterone is to prevent it from being converted (aromatized) into excess estrogen. Too much estrogen plays havoc with a man's sex life by binding to testosterone receptor sites and may contribute to the over-production of SHBG. SHBG binds free testosterone in a way that makes it unavailable to receptor sites in the brain, nerves and genitals.

Estrogen overload is a serious problem in aging men. One report showed that estrogen levels of the average 54-year-old man are higher than those of the average 59-year-old woman. Estrogen is a necessary hormone for men, but too much causes a wide range of health problems. High serum levels of estrogen also trick the brain into thinking that enough testosterone is being produced, thereby slowing the natural production of testosterone.

Based on the multiple deleterious effects of excess estrogen in men, aggressive actions should be taken to reduce estrogen to a safe range. To determine if estrogen levels are too high, men are encouraged to have their blood tested for estradiol. If the blood test results show estradiol levels are greater than 30 pg/mL, men should consider radical lifestyle changes, and/or taking an aromatase-inhibiting nutrient or drug.

A numerical example of the effects of a nutritional aromatase inhibitor can be seen on one of the subjects in the pilot studies whose initial serum estradiol level was a high 54 and free testosterone a moderately low 14.4. After only 30 days on a nutritional aromatase inhibitor, estradiol levels fell to 36 (from 54) and free testosterone levels increased to 22.5 (from 14.4). In this pilot study, funded by The Life Extension Foundation, 9 of 10 test subjects showed a significant decline in excess estrogen levels when several herbal extracts were combined. These kinds of results show how some men reduce excess estrogen while boosting free testosterone.

Herbs and male sexual potency

There are herbal extracts that have been shown to either increase or decrease testosterone levels.

Conversely, herbs that increase free testosterone and suppress excess estrogen are highly desirable for healthy men over age 40 who suffer the premature aging effects of a testosterone deficit, including loss of libido. We discuss some of these herbal extracts here.

Chrysin

A bioflavonoid called chrysin has shown potential as a natural aromatase-inhibitor. Chrysin can be extracted from various plants. Body builders have used it as a testosterone boosting supplement. The problem with chrysin is that because of its poor absorption into the bloodstream, it has not produced the testosterone enhancing effects users expect. In a study published in Biochemical Pharmacology (1999, Vol.58), the specific mechanisms of chrysin's absorption impairment were identified, which infers that the addition of a pepper extract (piperine) could significantly enhance the bioavailability of chrysin. Pilot studies have found that when chrysin is combined with piperine, reductions in serum estrogen (estradiol) and increases in total and free testosterone result in 30 days. Aromatase-inhibiting drugs are used to treat women with estrogen-dependant breast cancers. The rationale for this therapy is that estrogen is produced by fat cells via a process known as aromatization. Aging men often have excess aromatase enzyme activity, and the result is that too much of their testosterone is "aromatized" into estrogen. In a study published in the Journal of Steroid Biochemical Molecular Biology (1993;Vol 46, No 3), chrysin and 10 other flavonoids were compared to an aromatase-inhibiting drug (aminoglutethimide). The study tested the aromatase-inhibiting effects of these natural flavonoids (such as genistein, rutin, tea catechins, etc.) in human fat cell cultures. Chrysin was the most potent aromatase-inhibitor, and was shown to be similar

in potency and effectiveness to the aromatase-inhibiting drug. The scientists conducting the study concluded by stating that the aromatase-inhibiting effects of certain flavonoids may contribute to the cancer preventive effects of plant-based diets. Two recent studies have identified specific mechanisms by which chrysin inhibits aromatase in human cells. These studies demonstrate that chrysin is a more potent inhibitor of the aromatase enzyme than phyto-estrogens and other flavonoids that are known to have aromatase-inhibiting properties (Arch Pharm Res 1999 Jun;22(3):309-12; J Steroid Biochem Mol Biol 1997 Apr;61(3-6):107-15). The purpose of these studies was to ascertain which fruits and vegetables should be included in the diet of postmenopausal women to reduce the incidence of breast cancer. Excess levels of mutagenic forms of estrogen have been linked to a greater risk of breast cancer, and scientists are studying dietary means of naturally reducing levels of these dangerous estrogens. Flavonoids such as chrysin are of considerable interest because they suppress excess estrogen via their aromatase-inhibiting properties. While this cancer preventing effect is most important for women, inhibiting aromatase in aging men has tremendous potential for naturally suppressing excess estrogen while boosting low levels of testosterone to a youthful state.

Since chrysin is not a patentable drug, don't expect to see a lot of human research documenting its effects. There are lots of FDA approved drugs that inhibit aromatase (such as Arimidex), and there is not much economic interest in finding natural ways of replacing these drugs. While prescription aromatase-inhibiting drugs are relatively free of side effects, aging men who are seeking to gain control over their sex hormone levels often prefer natural sources, rather than trying to convince a physician to prescribe a drug (such as Arimidex) that is not yet approved by the FDA as an anti-aging therapy. (Arimidex is prescribed to estrogen-dependant breast cancer patients to prevent testosterone and other hormones in the body from converting, i.e. aromatasing, into estrogen.)

An advantage to using plant extracts to boost testosterone in lieu of drugs is that the plant extracts have ancillary health benefits. Chrysin, for example, is a potent antioxidant that possesses vitamin-like effects in the body. It has been shown to induce an anti-inflammatory effect, possibly through inhibition of the enzymes 5-lipoxygenase and cyclooxygenase inflammation pathways. Aging is being increasingly viewed as a pro-inflammatory process, and agents that inhibit chronic inflammation may protect against diseases as diverse as atherosclerosis, senility and aortic valve stenosis. Chrysin is one of many flavonoids being studied as a phyto-extract that may prevent some forms of cancer. If chrysin can boost free testosterone in the aging male by inhibiting the aromatase enzyme, this would provide men with a low cost natural supplement that could provide the dual anti-aging benefits of testosterone replacement and aromatase-inhibiting drug therapy.

As previously discussed, boosting free testosterone levels can have a dramatic effect on sex drive, performance and satisfaction. Pilot studies indicate that chrysin increases total and free testosterone levels in the majority of men who take it with piperine.

Chrysin has one other property that could add to its libido-enhancing potential. A major cause of sexual dissatisfaction among men is work-related stress and anxiety. Another problem some men have is "sexual performance anxiety" that prevents them from being able to achieve erections when they are expected to. In a study published in Pharmacology Biochemistry and Behavior (1994, Vol 47), mice were injected with diazepam (Valium), chrysin or placebo to evaluate the effects these substances had on anxiety and performance levels. Chrysin was shown to produce anti-anxiety effects comparable with diazepam, but without sedation and muscle relaxation. In other words, chrysin produced a relaxing effect in the brain, but with no impairment of motor activity. The mechanism of action of chrysin was compared to diazepam, and it was shown that unlike diazepam, chrysin can reduce anxiety without inducing the common side-effects associated with benzodiazepine drugs.

A common problem with benzodiazepine drugs is memory impairment. In a study published in a 1997 issue of Pharmacology Biochemistry and Behavior (Vol 58, No 4), chrysin displayed potent anti-anxiety effects in rats, but did not interfere with cognitive performance. In this study, diazepam was shown to inhibit neurological function, but chrysin (and other anti-anxiety flavonoids) had no effect on training or test session performance. The scientists conducting this study pointed out that chrysin selectively inhibits anxiety in the brain but, unlike diazepam, does not induce the cognitive impairment.

Chrysin may therefore offer libido-enhancing effects in the aging male by:

- Increasing free testosterone, - Decreasing excess estrogen, - Producing a safe anti-anxiety effect.

Chrysin is being sold to body builders by commercial supplement companies that do not know if their product is favorably modulating testosterone and estrogen levels in men. The Life Extension Foundation, on the other hand, has conducted meticulous studies to evaluate the effects of chrysin (combined with piperine to facilitate absorption) on aging men. These studies have produced some impressive preliminary data, and ongoing research will be reported in future issues of Life Extension magazine.

Nettle

About 90% of testosterone is produced by the testes, the remainder by the adrenal glands. Testosterone functions as an aphrodisiac hormone in brains cells, and as an anabolic hormone in the development of bone and skeletal muscle. But testosterone that becomes bound to serum globulin is not available to cell receptor sites and fails to induce a libido effect. It is, therefore, desirable to increase levels of "free testosterone" in order to ignite sexual arousal in the brain.

As discussed already, a hormone that controls levels of free testosterone is called sex hormone-binding globulin (SHBG). When testosterone binds to SHBG, it loses its biological activity and becomes known as "bound testosterone," as opposed to the desirable "free testosterone." As men age past year 45, SHBG's binding capacity increases almost dramatically-by 40% on average-and coincides with the age-associated loss of libido.

Some studies show that the decline in sexual interest with advancing age is not always due to the amount of testosterone produced, but rather to the increased binding of testosterone to globulin by SHBG. This explains why some older men who are on testosterone replacement therapy do not report a long-term aphrodisiac effect. That is, the artificially administered testosterone becomes bound by SHBG, and is not bioavailable to cellular receptor sites where it would normally produce a libido-enhancing effect.

It should be noted that the liver also causes testosterone to bind to globulin. This liver-induced binding of testosterone is worsened by the use of sedatives, anti-hypertensives, tranquilizers and alcoholic beverages. The overuse of drugs and alcohol could explain why some men do not experience a libido-enhancing effect when consuming drugs and plant-based aphrodisiacs. An interesting review, "How Desire Dies" (Nature, 381/6584, 1996), discusses how frequently prescribed drugs, such as beta-blockers and antidepressants, cause sexual dysfunction. Prescription drugs of all sorts have been linked to inhibition of libido.

Logically, one way of increasing libido in older men would be to block the testosterone-binding effects of SHBG. This would leave more testosterone in its free, sexually activating form.

A highly concentrated extract from the nettle root provides a unique mechanism for increasing levels of free testosterone. Recent European research has identified constituents of nettle root that bind to SHBG in place of testosterone, thus reducing SHBG's binding of free testosterone. As the authors of one study state, these constituents of nettle root "may influence the blood level of free, i.e. active, steroid hormones by displacing them from the SHBG bindings site."

The prostate gland also benefits from nettle root. In Germany, nettle root has been used as a treatment for benign prostatic hyperplasia (enlargement of the prostate gland) for decades. A metabolite of testosterone called dihydrotestosterone (DHT) stimulates prostate growth, leading to enlargement. Nettle root inhibits the binding of DHT to attachment sites on the prostate membrane.

Nettle extracts also inhibit enzymes such as 5 alpha reductase that cause testosterone to convert to DHT. It is the DHT metabolite of testosterone that is known to cause benign prostate enlargement, excess facial hair and hair loss at the top of the head.

Muira puama

French scientists have identified an herbal extract that has shown libido enhancing effects in two human clinical studies. Muira puama comes from the stems and roots of the Ptychopetalum olacoides plant, and is widely used in the Amazon region of South America as an aphrodisiac, tonic and cure for rheumatism and muscle paralysis.

Muira puama has been the subject of two published clinical studies conducted by Dr. Jacques Waynberg, an eminent medical sexologist and author of 10 books on the subject. The first study, conducted at the Institute of Sexology in Paris under Waynberg's supervision, was reported in the November 1994 issue of The American Journal of Natural Medicine. The study population consisted of 262 men complaining of lack of sexual desire, or inability to attain or maintain erection. After two weeks, 62 percent of patients with loss of libido rated the treatment as having a dynamic effect, while 52 percent of patients with erectile dysfunction rated the treatment as beneficial. The article goes on to compare muira puama favorably to yohimbine, stating, "Muira puama may provide better results than yohimbine without side effects."

Dr. Waynberg's second study, entitled "Male Sexual Asthenia," focused on sexual difficulties associated with asthenia, a deficiency state characterized by fatigue, loss of strength, or debility, all symptoms of a testosterone deficiency. The study population consisted of 100 men over 18 years of age who complained of impotence or loss of libido, or both. A total of 94 men completed the study and were evaluated. Muira puama treatment led to significantly increased frequency of intercourse for 66% of couples. Of the 46 men who complained of loss of desire, 70% reported intensification of libido. The stability of erection during intercourse was restored in 55% of patients and 66% of men reported a reduction in fatigue. Other beneficial effects included improvement in sleep and morning erections.

Treatment with muira puama was much more effective in cases with the least psychosomatic involvement. Of the 26 men diagnosed with common sexual asthenia without noticeable sign of psychosomatic disorder, the treatment was effective for asthenia in 100% of cases, the lack of libido in 85% of cases, and for inability of coital erection in 90% of cases.

The latter finding confirms that broad tonic action of muira puama on conditions of fatigue and stress related sexual dysfunction. Since muira puama is not an artificial stimulant, it fortifies the system over a period of time. Some men report increased vitality within two weeks, while the full effects build over several weeks.

Dr. Waynberg notes that his toxicology studies and observations corroborate the conclusions of the scientific literature on the absence of toxicity of muira puama, which is well tolerated by men in general good health.

One of the earliest scientific studies of muira puama was conducted by another French doctor, Dr. Rebourgeon. His research found the plant to be effective in "gastrointestinal and circulatory asthenia as well as impotence." Three of the most respected scientific authorities on medical herbalism recommend muira puama. In newly published books, James Duke, Ph.D., Chief of the United States Department of Agriculture's Medical Plant Laboratory, and Michael Murray, M.D., recommend muira puama for erectile dysfunction or lack of libido. In addition, Daniel Mowrey, Ph.D., states the following in his book Herbal Tonic Therapies (p. 358):

Few in number are the plants that seem to have a reliable reputation as true aphrodisiacs. . . . Snake oil remedies abound, and confusion, dishonesty and hyped-up placebo razzmatazz carry the day. Out of this mess, one plant, virtually unknown to most Americans, appears to have risen above the competition. The plant is called muira puama. And though not much is known scientifically about the plant, all indications would lead one to believe that here is a material with the potential for making an important and significant contribution to the health of the male reproductive system.

Based on the clinical reports documenting the libido and energy enhancing effects of muira puama, it is possible that this herb induces these positive changes by favorably altering the hormone balance in aging men, i.e. increases free testosterone and/or suppresses excess estrogen.

Putting it all together

Enhanced sexual enjoyment is of paramount importance to a great many people, increasingly so as we age. An enormous amount of published data documents the libido-enhancing effects that occur when testosterone is restored to a youthful level.

Testosterone is much more than a sex hormone. There are testosterone receptor sites in cells throughout the body, most notably in the brain and heart. Youthful protein synthesis for maintaining muscle mass and bone formation requires testosterone. Testosterone improves oxygen uptake throughout the body, helps control blood sugar, regulate cholesterol and maintain immune surveillance. The body requires testosterone to maintain youthful cardiac output and neurological function.

Men suffering from depression often have lower levels of testosterone than control subjects. For some men, elevating free testosterone levels could prove to be an effective anti-depressant therapy. There is a scientific basis for free testosterone levels being measured in men suffering from depression and replacement therapy initiated if free testosterone levels are low normal or below normal.

One of the most misunderstood hormones is testosterone. Body builders tarnished the reputation of testosterone by putting large amounts of synthetic testosterone drugs into their young bodies. Synthetic testosterone abuse can produce detrimental effects, but this has nothing to do with the benefits a man over age 40 can enjoy by properly restoring his natural testosterone to a youthful level.

The many health benefits of hormone modulation therapy in aging men is the subject of these books authored by highly respected medical doctors: Vitality and Potency, by Jonathan V. Wright, M.D. and Lane Lenard, Ph.D. and The Testosterone Syndrome, co-authored by Eugene Shippen, M.D. These books provide meticulous molecular details, along with many case histories relating to the sexual enhancing effects that occur when free testosterone is increased beyond normal "middle-aged" levels.

In the November 1999 issue of this publication, an in-depth article described complex pharmaceutical methods of increasing free testosterone using FDA approved drugs. Many members, however, inquired about natural ways of increasing testosterone while suppressing excess estrogen.

Ongoing research at The Life Extension Foundation has resulted in several plant extracts being identified that appear to increase free testosterone and suppress excess estrogen in most men. In addition, clinical studies on one of these plant extracts indicates a significant libido-enhancing effect in the majority of men in placebo-controlled trials.

Men over age 40 now have the option of using testosterone patches or creams that need to be prescribed by their physician, or they can try a new combination of plant extracts that have shown promising results.

Results from published studies continue to substantiate the critical role that testosterone plays in protecting against premature aging. Life Extension magazine readers will be kept informed on scientifically validated testosterone enhancing strategies in future issues.

Excess Estrogen and age-associated immune dysfunction

It is well known that aging results in the shrinkage of the thymus gland, along with a reduction in the secretion of thymic hormones and T-cells, all of which are essential for maintaining youthful immune synchronization.

A study published in the journal Immnological Reviews (1997, Vol 160) showed that excess estrogen may be the primary sex hormone responsible for age-induced thymic involution (shrinkage) and age-associated immune dysfunction. The name of this extensive study was "Thymic Aging and T-Cell Regeneration," and it suggested that hormone modulation was one way of accomplishing thymic regeneration.

A chapter from the 1998 textbook Principles and Practices of Geriatric Medicine entitled "Immunity and Aging" also discussed the role sex steroid hormones play in thymic involution.

These studies suggest that restoring youthful sex hormone profiles could assist in protecting against immune impairment caused by the shrinking thymus gland.

Hormone modulating nutrients: the studies

As described in the November 1999 issue of Life Extension magazine, there are testosterone drugs and estrogen suppressing drugs that can be prescribed by your doctor. Understandably, however, some people do not want to use drugs if nutrients can accomplish the same objective.

In order to ascertain the safety and efficacy of various nutrients that are purported to modulate male hormone levels, The Life Extension Foundation has been sponsoring clinical studies to assess the effects of specific supplements on blood levels of testosterone, estrogen, SHBG, etc.

The results from the first pilot study showed that nine out of 10 men experienced a significant reduction in serum estradiol (estrogen) levels after only thirty days, compared to baseline. In this brief study, total testosterone increased in seven out of 10 men, but free testosterone increased in only four of the 10 men studied. Other blood parameters were not statistically altered.

A more comprehensive study incorporating a different combination of nutrients resulted in 8 out of 8 men experiencing increases in free testosterone while levels of the undesirable SHBG declined in seven out of eight men, compared to baseline. Estrogen and other blood parameters were not significantly altered in this study.

A third study was undertaken to evaluate still another combination of nutrients. It revealed that after thirty days, 12 out of 17 men experienced an increase in total testosterone and 11 out of 17 showed an increase in free testosterone, compared to baseline. Again, other blood parameters were not significantly altered.

Clinical trials are ongoing, and are expected to continue into early year 2000.

Medical Testing

For the average male over age 40, increasing free testosterone can restore the sexual fire of youth. The only downside to increasing free testosterone levels to those of a healthy 21-year-old is the potential effects it may have on men with prostate cancer. Before embarking on a testosterone-enhancement program a baseline blood PSA test and a digital rectal exam taken to rule out existing prostate cancer. When using testosterone drugs, PSA blood tests should be taken every 30-45 days for the first five months to rule out hidden prostate cancer.

When using slower acting testosterone boosting nutritional supplements, PSA testing can be reduced to every 60-90 days for the first eight months. Remember, the preponderance of the published literature shows that increasing free testosterone does not increase the risk of cancer in healthy men, but those with existing prostate cancer should avoid testosterone boosting drugs and supplements.

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