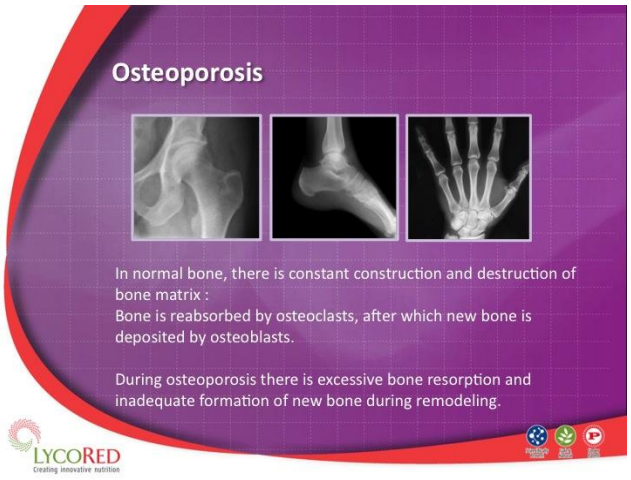
Lyc-O-Fem™

The Natural Approach to Menopause

Menopause: A Natural Biological Event in Every Woman's Life

Sometime during mid-life every woman will enter into perimenopause. This is a period lasting a number of years during which a woman's estrogen level decreases and monthly periods may be erratic. Typically, when a woman is in her late forties or early fifties her ovaries stop releasing eggs signaling the end of fertility and the onset of menopause. During the perimenopause transition, a woman may experience a number of uncomfortable symptoms connected to the ebbing of estrogen. These discomforts can continue well into the post-menopausal years and may be severe enough to disrupt a woman's daily activities and sense of well-being. The most common symptoms, hot flashes and night sweats, are due to vasomotor instability. Mood changes are also typical. The significant reduction in circulating estrogen during and after menopause also puts a woman at increased risk of bone loss.

Menopause and Bone Health



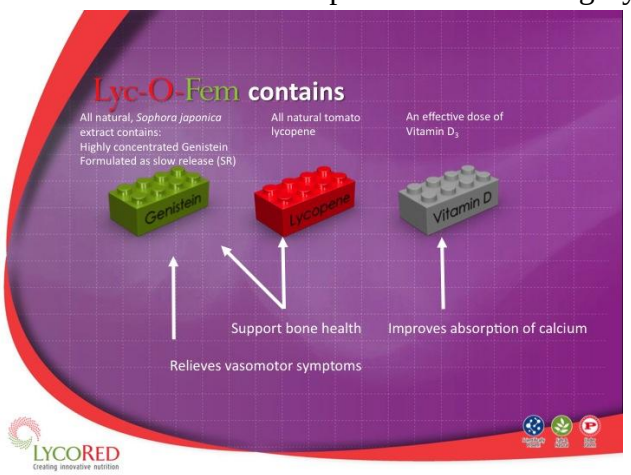
The decreased estrogen levels that characterize menopause have been linked to bone loss and osteoporosis, a medical condition in which the bones become brittle. Osteoporosis occurs when the body fails to produce enough new bone, too much existing bone is reabsorbed, or both. The underlying mechanism of postmenopausal osteoporosis is an imbalance between bone resorption by osteoclasts and bone formation by osteoblasts. Osteoporosis is estimated to affect 200 million women worldwide: approximately one-tenth of women age 60, one-fifth of women age 70, two-fifths of women age 80 and two-thirds of women age 90 (1).

Some women glide through this menopausal life transition with relative ease, but for others the discomforts may be disabling and the risk of bone loss of great concern. While there are

pharmaceutical options, many women prefer to take a natural approach to menopause management. For these women, Lyc-O-Fem™, a natural dietary supplement, provides a welcome assist.

Lyc-O-Fem™: Natural Menopause Management

Lyc-O-Fem is the first in LycoRed's new line of innovative products combining pure genistein, tomato lycopene and an effective dose of vitamin D_3. These three ingredients work together to support bone health and strength. Lyc-O-Fem is protected by multi-layered patents and is differentiated from other products in the category by its unique composition.



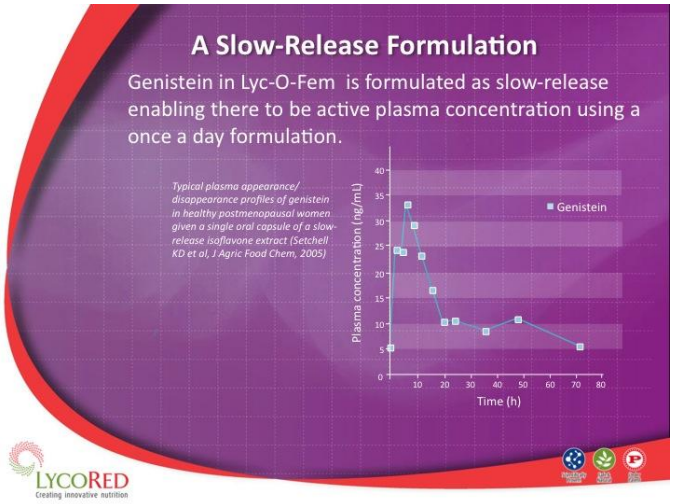
Lyc-O-Fem is formulated using slow-release technology that enables the body to maintain a constant level of genistein throughout the day. The slow release of the genistein means that it can be supplied in just one daily serving. This is important for overall effectiveness. Women are more likely to consistently comply with a one-per-day regimen.

Innovative Formulation

The highly concentrated Japanese pagoda tree (*Sophora japonica*) extract in Lyc-O-Fem is standardized to provide 98% genistein and formulated as slow-release. Genistein is an isoflavone, a non-steroidal compound. Isoflavones bear a structural similarity to estradiol (the major form of estrogen in human beings), and they act in the body in a similar manner (2). Because isoflavones are constituents of plants, they are called phytoestrogens. Plant sources of isoflavones include soy, red clover and kudzu as well as the Japanese pagoda tree. Lyc-O-Fem™ is soy-free and therefore an acceptable product for people with soy allergies.

The lycopene in Lyc-O-Fem is a carotenoid with potent antioxidant properties. It is extracted from specially cultivated ripe tomatoes in a very gentle process designed to protect the sensitive natural phytochemicals from damage. Lycopene has been shown to have a beneficial effect on bone health.

Vitamin D can be synthesized in the body by exposure to UV-radiation from the sun. The synthesis of vitamin D in the skin through the action of sunlight is insufficient to meet the daily requirements of people living in countries where there is little sunlight exposure during winter months. Vitamin D deficiency is associated with low bone mineral density, a key risk factor for osteoporotic fracture. Vitamin D can be obtained from food or ingested as vitamin D_2 (ergocalciferol) or vitamin D_3 (cholecalciferol) supplements. Vitamin D is highly susceptible to oxidation, therefore, the vitamin needs to be formulated in a way that protects the active ingredient. LycoRed uses different technologies to ensure highly stable vitamin D_3 formulations. In humans, the principal physiological function of vitamin D_3 is to maintain serum calcium and phosphorus concentrations in a range that supports cellular processes, neuromuscular function, and bone formation or ossification. Vitamin D_3 accomplishes this goal by enhancing the efficiency of the small intestine in absorbing dietary calcium and phosphorous and by mobilizing calcium and phosphorus from the bone.



Lyc-O-Fem™ Supports Strong Healthy Bones

There are a variety of compounds classified as isoflavones. A review of current literature based on new (preclinical and clinical) data indicates that the aglycone genistein appears to be the most effective isoflavone at helping to prevent bone loss and restore bone. This is the isoflavone found in the Lyc-O-Fem formulation. Genistein aglycone can regulate bone cell metabolism so as to rebalance bone turnover in the direction of bone formation. Genistein stimulates osteoblasts and inhibits osteoclasts mainly through the osteoprotegerin-sRANKL system.

A double blind placebo controlled study of post-menopausal women showed significant increase in bone mineral density (BMD) at the femoral neck after 12 months of daily administration of 55 mg genistein isolated from soy (3). A large clinical trial has studied the effects of genistein on bone metabolism in post-menopausal women. Over a 2 year period, supplementation with 54

mg/day of genistein aglycone was shown to regulate bone metabolism significantly increasing femoral neck and lumbar spine BMD (4, 5). In an extension of this study, a sub-cohort of 138 osteopenic, postmenopausal women tested the continued safety profile of genistein aglycone at a dosage of 54 mg/day and its effects on bone metabolism. After 3 years of therapy, genistein exhibited a promising safety profile in this study (6).

It should be noted that while epidemiological studies assessing the skeletal effects of soy foods and soy dietary supplements rich in isoflavones on Asian women consuming typical Asian diets suggest a beneficial skeletal effect, (7) clinical trials have yielded some conflicting results. There are a number of possible explanations for this variability. Clinical trials assessing the effects of soy isoflavones on bone mineral density and bone turnover markers in premenopausal and postmenopausal women(7) have employed a wide variety of intervention products with markedly varying isoflavone content. These have included traditional soy foods, isolated soy protein (ISP), soy extracts and isolated isoflavones, each with a variety of controls (8). This variation could account for the differing results. More controlled studies are needed to determine the levels at which isoflavones are most effective.

Tomato lycopene also plays an important role in supporting bone health. Laboratory studies have shown that lycopene inhibits formation of osteoclasts and associated bone resorption. Furthermore, lycopene stimulates proliferation and differentiation of osteoblasts suggesting an anabolic effect. Lycopene was found to enhance estrogenic activity in bone cells but inhibit it in breast cancer cells (9).

A 17 year longitudinal study on the correlation between carotenoid intake and risk for hip fracture in post-menopausal women demonstrated a protective effect of high lycopene plasma levels equivalent to a dietary intake of approximately 12 mg/day of lycopene consumption (10). The effect of short term restriction of lycopene from the diet on bone turnover biomarkers was tested in post-menopausal women (11). In this study it was shown that low levels of plasma lycopene are associated with increased levels of NTx, a biomarker used to measure the rate of bone turnover. This result indicates that lycopene deprivation results in an increased bone turnover. Lycopene supplementation may decrease bone resorption in postmenopausal women and may, therefore, be beneficial in reducing the risk of osteoporosis.

In another placebo-controlled study (11), the effect of four months of lycopene supplementation on bone turnover was tested in post-menopausal women. Three groups of fifteen women were supplemented with either tomato juice (30 mg lycopene), lycopene-enriched tomato juice (70 mg lycopene), or a proprietary tomato extract (30 mg lycopene). When compared to placebo no effect was detected due to the small sample size. However, when measuring the results for all forty-five women as a single group, a significant reduction in NTx levels was observed suggesting a positive effect of lycopene on bone health.

Vitamin D is biologically inactive and requires successive hydroxylations, first in the liver, where 25-hydroxyvitamin D (25-OHD) is formed, and then in the kidneys where 1,25-dihydroxyvitamin D (1,25-(OH)2D), the biologically active form of vitamin D is produced. Observational studies have shown a positive association between serum 25-hydroxyvitamin D (range 40–90 nmol/L) and higher bone density (12). In older women (> 65 years), daily intake of 700 or 800IU of vitamin D_3 resulted in small but significant increases in bone mineral density in the lumbar spine and femoral neck relative to placebo (13). Similarly, in a subgroup of 2431 women taking vitamin D and calcium supplements, the Women's Health Initiative found a 1.06% increase in total hip density ($p < 0.001$) (14).

Lyc-O-Fem™ Offers Relief from Menopausal Discomfort

Five studies, involving a total of 177 treated participants supplemented with well-characterized isoflavone containing products providing more than 15 mg genistein (calculated as aglycone equivalents) per treatment, reported a statistically significant decrease in hot flash symptoms (15). Typical isoflavone intake has been estimated at around 15-50 mg/day in women living in Asian countries, especially China and Japan. This intake level provides an optimal serum concentration of phytoestrogens (16).

Meta-analysis revealed that ingestion of soy isoflavones (median, 54 mg; aglycone equivalents) for six weeks to twelve months, significantly reduced the frequency of hot flashes by 20.6% compared with placebo. Meta-analysis also revealed that isoflavones significantly reduced hot flash severity by 26.2% compared with placebo. Isoflavone supplements providing more than 18.8 mg of genistein (the median for all studies) were more than twice as effective at reducing hot flash frequency as supplements containing lower levels of genistein (17).

A recent review looked at nineteen randomized, placebo controlled clinical trials studying soy-derived isoflavones (dietary, extract or concentrate) in women suffering from VMS (18). Overall, these published studies demonstrated a high heterogeneity in efficacy making it difficult to reach a conclusion as to whether soy-derived genistein is effective in reducing hot-flashes. The high rate of placebo effect in studies involving hot flashes in post-menopausal women also adds to the complexity of the issue. More well controlled studies are needed in this very promising area of menopausal support.

Conclusions

The unique slow release Lyc-O-Fem formula provides a natural way for women to address the concerns of menopause. Lyc-O-Fem helps to relieve the hot flashes and nights sweats that afflict so many women at this stage of life. At the same time, Lyc-O-Fem enables menopausal women to be proactive in supporting the health and strength of their bones. The slow release delivery of Lyc-O-Fem's key ingredient allows women to obtain the results they're looking for from a convenient one per day supplement.

Lyc-O-Fem™ is a product of LycoRed Ltd, the company committed to bringing the highest quality science-based products to market.

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