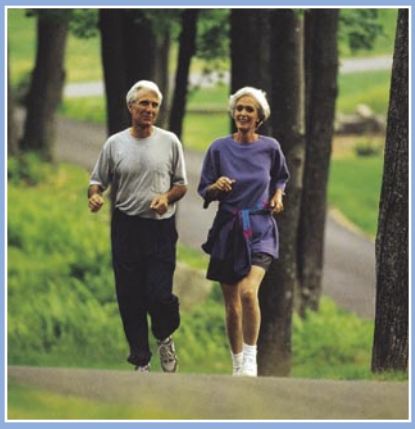
totalhealth

Special Report

BioSil™—Collagen and the Health of the Skin and Bones



BioSil™ and the Collagen Connection

by Dallas Clouatre, Ph.D., and Kevin M. Connolly, Ph.D.

Welcome to this ***totalhealth*** special report on choline-stabilized orthosilicic acid.

The object of these reports is to offer you, a committed health food supplement consumer, cutting-edge information on nutraceutical ingredients and products that can support your personal needs.

Currently, osteoporosis and arthritis are two of the most active categories of supplements sales. In general, bone, joint, and connective tissue problems are among the most common health issues that trouble individuals as they age. Concern with these conditions obviously will increase as the "baby boom" generation matures. By the year 2010, almost a third of the population of the U.S. will be aged 50 years or older. Bone, joint and connective tissue problems also affect athletes and others who exercise regularly and vigorously.

One of the most significant products for supporting the health of bones, joints and connective tissues, as well as that of skin, hair and nails, is biologically active silicon, the form of silicon known as orthosilicic acid.

Silicon, in its biologically active form orthosilicic acid, is intimately involved in the growth and repair of all of the structural tissues found in the body because of its role in the biosynthesis of collagen.

Approximately 28 percent of bone is collagen. Research shows that supplementing with stabilized orthosilicic acid stimulates the synthesis of collagen and leads to enhancements in the repair of tissue based on collagen. It both increases the amount of calcium available in the circulation for deposit in the bones and increases actual bone density. This has now been shown clinically.

Many of the same factors that protect the health of the cartilage of the joints will influence the health of the bones, and vice versa.

Supplementation with orthosilicic acid is also a powerful means of improving skin regeneration. Orthosilicic acid supplementation (as BioSil) in animal studies has been shown to increase the collagen concentration in the dermis by up to 12.5 percent. Because silicon is crucial for the activation of the enzymes responsible for the cross-linking in collagen, supplementation not only speeds the regeneration of this protein but also increases its strength and elasticity. A recent human trial proved that the result is better skin with fewer wrinkles. Similar benefits are realized with the hair and nails, as well.

Stabilized concentrated orthosilicic acid is marketed exclusively by Jarrow Formulas under the name BioSil.

Lyle Hurd

Publisher/edtior, ***totalhealth*** magazine

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Kevin M. Connolly, Ph.D. (UCLA), is the Director of Scientific Affairs at Jarrow Formulas, Inc. A newcomer to the dietary supplement industry, his previous experience is in basic biochemistry research, in which he had spent nearly 15 years in elucidating such diverse mechanisms as bacterial antibiotic resistance and collagen synthesis. He is an inventor whose name appears on several medical device patents and is a frequent guest on radio health programs throughout the country.

Choline-stabilized Orthosilicic Acid (BioSil™)

BioSil™ is choline-stabilized orthosilicic acid. It is a biologically active compound composed of silicon and the essential nutrient choline that has clinically proven health-promoting properties. Silicon (Si) is a conditionally essential element in plant, animal and human nutrition. It is important for the growth, development and regeneration of connective tissue (skin, cartilage, bones, etc.), hair, nails, and certain membranes, such as mucosal tissues. Both an unbalanced diet and the processing and refining of foods (such as the removal of fiber) can lead to substantially lower silicon content. Moreover, the levels of silicon in certain tissues generally decline with age.

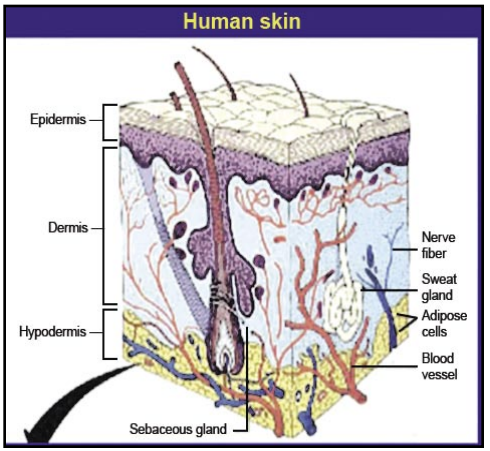
Most silicon found in foods and in dietary supplements is present as polymerized forms of orthosilicic acid (OSA). This means that the silicon is bound into chains with from two to many links. OSA is a water-soluble form of silicon and it is the molecular form in which silicon is found in the serum fraction of human blood. Only a small proportion of polymerized OSA is converted to OSA in the stomach. The success of the digestive system in making OSA available for assimilation is highly dependent upon the amount of hydrochloric acid being produced, and this aspect of digestion declines dramatically as we age.

The availability of silicon in its biologically active form—orthosilicic acid—is especially important to the health of the skin and bones. This is because in humans OSA is crucial for the synthesis of collagen, which is a primary structural component of the skin, bones and all connective tissues. Indeed, collagen accounts for approximately one third of the total amount of protein found in the human body.

Until recently, enhancing silicon nutrition sufficiently to realize benefits has not been a simple matter. Only very diluted concentrations of the orthosilicic acid molecule are found in nature, such as in mineral-rich spring water, due to the very limited stability of the molecule in its non-polymerized form. Changes in food sources of OSA, and the difficulties faced in extracting it from foods, particularly as we age, suggest that dietary supplementation is advisable. New technology that makes this possible has been developed to stabilize and concentrate OSA using choline. Choline is an essential nutrient important in the manufacture of some of the main components of cell membranes, such as phosphatidylcholine; hence, it supports the benefits of orthosilicic acid in choline-stabilized orthosilicic acid (ch-OSA™). The use of choline to create choline-stabilized orthosilicic acid allows the provision of a highly concentrated source of OSA useful in supporting nutrition targeted towards the health of all collagen-dependent tissues. The two most prominent of these tissues are the skin and the bones. ■

BioSil for Healthy Skin

The skin is your largest organ, yet it is the organ most likely to be taken for granted. An adult's skin is 15 to 20 percent of total body weight. Each square centimeter has 6 million cells, 5,000 sensory points, 100 sweat glands, and 15 sebaceous glands. A skin cell is born in the lower layer of the skin called the dermis, which is supplied with blood vessels and nerve endings. The top layer of the dermis is the *papillary* layer. As scrapes and abrasions regularly remind us, this layer contains blood vessels and nerve endings. The bottom layer of the dermis is called the *reticular* layer, and it is here that the oil glands and hair follicles are found.



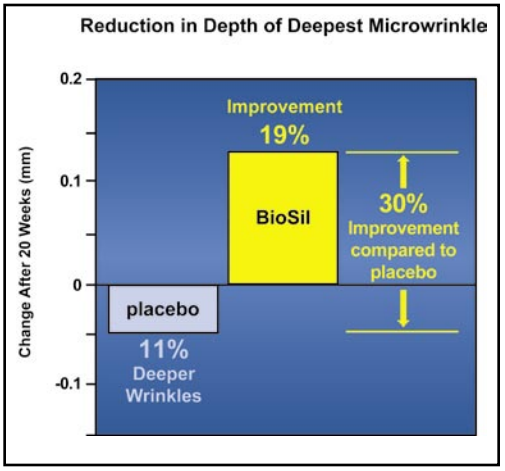
Cross-section of skin showing the epidermis and the dermis

The condition of the collagen and elastin in these two layers primarily determines the appearance and resiliency of the skin. Proper amounts of collagen in these layers are responsible for the skin's strength and ability to retain moisture. Natural or premature aging (due to UV exposure) of the skin leads to marked decreases in collagen, glycosaminoglycans (GAG), and proteoglycan content. These alterations lead to dramatic changes in skin elasticity, moisture content and its ability to serve as a barrier against the environment.

It has long been established that silicon is an important factor for the synthesis of collagen and can exert this activity in the preservation of healthy skin. It should be pointed out that most recent studies on the health roles of silicon (orthosilicic acid), particularly human clinical studies, have utilized choline-stabilized orthosilicic acid. In animals, supplemental choline-stabilized orthosilicic acid has been shown to increase skin collagen content. However, not established until recently is whether fundamental improvements can be made in skin that has aged prematurely or has been photodamaged (i.e., damaged by exposure to excessive sunlight). According to conventional wisdom, although topical creams as moisture barriers can keep the skin more hydrated, no fundamental improvements can be made in aged or sun damaged skin structure.

To find out whether this conventional wisdom is true, researchers put it to the test. In a clinical trial recently published by Barel, et al. in *Archives of Dermatological Research* (2005), fifty women between 40 and 65 years old with symptoms of aging facial skin were divided into two groups. One group ingested a placebo, two capsules per day, for 20 weeks. The second group

took two capsules per day of choline-stabilized orthosilicic acid (BioSil) supplying a total of 10 mg silicon for the 20-week period. No other anti-wrinkle treatment was followed. Researchers examined changes in skin roughness, elasticity and structure. Brittleness of the nails and hair also was measured.



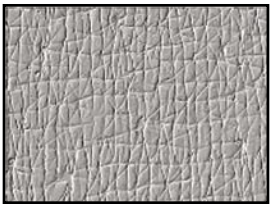
Twenty weeks of supplementation with BioSil by women with aging and photodamaged skin led to a reduction in the depth of the shallow wrinkles used as test markers. Based on Barel, et al. (2005) *Arch. Dermatol Res,* 297, 147–153.

Women taking the BioSil capsules experienced a significant improvement in skin elasticity compared with those taking the placebo. Similarly, women using BioSil exhibited 30 percent less skin roughness compared with the control group, that is, a 30 percent reduction in microwrinkle depth compared with placebo. All of these results were statistically significant improvements amongst the volunteers in the BioSil group compared with the control group.

Young skin is smooth, tight and resilient—in other words, elastic. Elasticity is a result of optimal collagen structure and water content in the underlying tissues. Collagen fibers provide most of the tensile strength of the body's structures. Young skin is characterized by a dense and well-organized network of collagen fibers with a rich pattern of intersections. It is this fine crosshatch network of strands that provides elasticity and holds moisture. Aging skin is characterized by a loss of elasticity resulting from collagen deficiency and a lack of water content in the underlying tissues. It also is characterized by a poor and disorganized collagen network that results in fewer, but deeper lines. These deeper lines further develop into visible wrinkles. Researchers often examine these changes by looking at a "microrelief" of the skin. Wrinkling in the "primary, secondary and tertiary lines" refers to the microrelief. Wrinkles in the microrelief level of skin, often referred to as "micro-wrinkles," develop over time into deeper, more visible wrinkles. If an oral or topical skin care product is effective, one will always notice the effects first on micro-wrinkles.

What the before-and-after microrelief of the skin shows is a change in the nature of the underlying collagen network of the skin. Dermatological studies have found that both photodamage and natural aging cause a reduction in the amount of procollagen in the skin, with a greater reduction due to aging. This means that the basic building block for collagen strands is reduced. The result is

Microrelief of the Skin

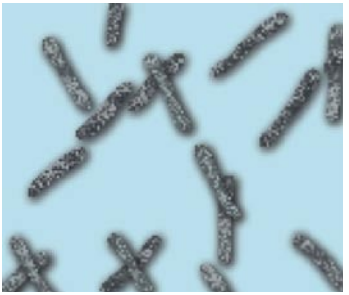


Before: **at the start of the study**

After: **following 20 weeks supplementation with BioSil. Visibly, skin is tighter and smoother looking with a reduction in the depth of wrinkles.**

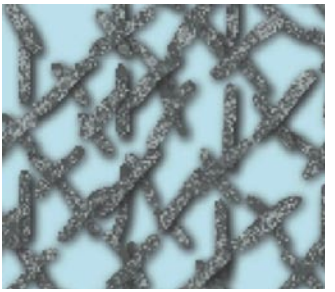
Based on Barel, et al. (2005) Arch. Dermatol Res, 297, 147–53.

Schematic Drawing of the Skin's Collagen Network



Aging Skin

Disorganized collagen network forming weak weave or broken crisscross pattern



Young Skin

Dense, well-organized network with many intersections and a tight weave pattern

a disorganized collagen network, greater roughness and less elasticity.

Twenty weeks of supplementation with BioSil (ch-OSA) helped return skin to a more youthful state with shallower wrinkles, resulting in a clinically significant improvement in skin texture and resilience. According to principal investigator, André Barel, "This is promising news for women who want a safe, non-invasive way to address the effects of sun damaged or prematurely aging skin…. This work indicates that using [ch-OSA] may represent a viable oral treatment, and an alternative or complementary treatment to topical products." ■

BioSil and Bone Health

For years, calcium has received most of the publicity when it comes to bone health; but that is changing. Deposited minerals comprise only 60 percent of the total weight of bone. The rest is water and a living collagen-based matrix. The matrix or osteoid of mostly collagen gives bone its overall form and flexibility. It acts as a scaffolding system to provide support and to hold bone minerals in place. This three-dimensional network is filled with a mineral component of calcium-phosphorous crystals (hydroxyapatite; $Ca10(PO4)6(OH)2$) that stiffen and strengthen the matrix. Embedded into this protein-mineral matrix are three types of cells that are responsible for the maintenance, growth and remodeling of the bone: osteoblasts, which create osteoid and initiate its mineralization; osteoclasts, which break down and recycle mineralized bone; and osteocytes, which aid bone maintenance. Many bone specialists now believe the quality of the bone matrix is even more important in preventing fractures than is the degree of mineralization (bone mineral density, or BMD). Bio-available silicon plays an important role in the bone collagen matrix, a point demonstrated with OSA and choline-stabilized orthosilicic acid in both *in vitro* and *in vivo* trials.

Only about 30 years ago was it first recognized that silicon is a factor in bone calcification. Subsequent observations in a variety of animals have shown that silicon is instrumental in supporting bone and joint health. Again, this is because bone consists of crystals of the calcium-phosphorus mineral *apatite* imbedded in a matrix of the fibrous collagen protein and amino sugars. Approximately 28 percent of bone consists of collagen, mostly type I, and another 3 percent is glycosaminoglycans.

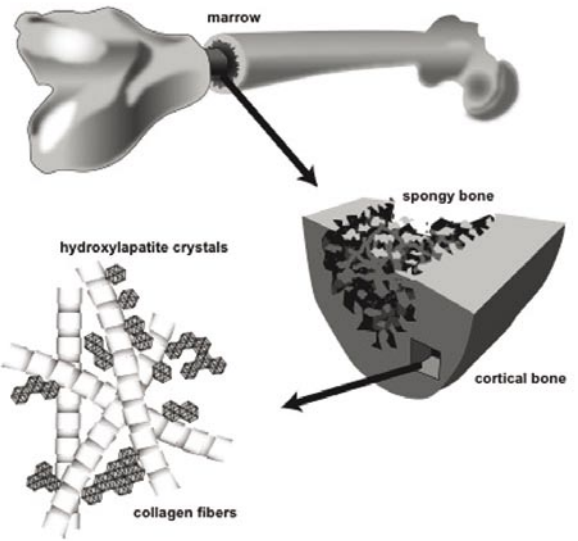
Inasmuch as choline-stabilized orthosilicic acid has been shown to stimulate collagen synthesis, it should come as no surprise that supplemental choline-stabilized orthosilicic acid stimulates the formation of the osteoid as well. Recent studies have confirmed that orthosilicic acid increases the synthesis of type-I collagen in osteoblasts, and stimulates the activity of prolyl hydroxylase enzymes to aid in the conversion of newly synthesized collagen protein into mature collagen fibrils. Collagen in bone is connected closely to the issue of bone quality, the flexibility and resilience of bone.

Bone quantity also involves dietary silicon. Scientists now are beginning to look at the connection between silicon status and bone mineral density in humans. An analysis of data from the Framingham Offspring cohort for 1,251 men and 1,596 pre- and post-menopausal women (aged 30–87 years) strengthens the silicon status/bone mineralization connection. Dietary silicon intake had a positive correlation with BMD at four sites in the hip in men, pre-menopausal women and post-menopausal women on hormone

replacement therapy. The analysis revealed up to a 10 percent difference in BMD between individuals with the highest (>40 mg Si/day) and lowest (<14 mg Si/day) intakes of dietary silicon.

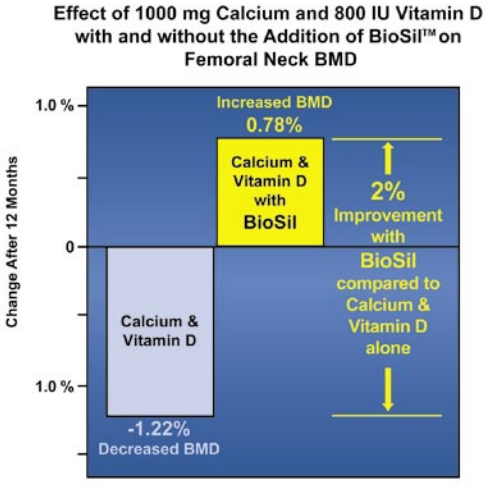
However, is silicon beneficial to women already losing bone mass, and is this benefit beyond that derived from calcium and vitamin D supplementation? It turns out that the answer to both these questions is "yes." Choline-stabilized orthosilicic acid (BioSil) has been shown to provide significant benefits in cases of low bone mineral density and to provide benefits significantly greater than those found with calcium and vitamin D supplementation alone.

A research team led by Professor T.D. Spector from St. Thomas Hospital in London conducted a clinical investigation that followed 114 women (mean age of 61) divided into four groups in which all groups received daily 1000 milligrams calcium and 800 IU vitamin D3, and the three test arms additionally received different amounts of choline-stabilized orthosilicic acid (BioSil). These were women already suffering from either osteopenia (reduced bone mass) or the more severe osteoporosis.



Approximately 28 percent of bone consists of collagen, mostly type I, and another 3 percent is glycosaminoglycans. Collagen is a primary component of the bone matrix.

At the end of 12 months, spinal BMD had not changed significantly. However, analysis of a subgroup (81 women) whose femur T score was less than -1 at the start of the study showed that volunteers taking 6 mg of silicon in the form of choline-stabilized orthosilicic acid per day exhibited a significant improvement in BMD in the neck of



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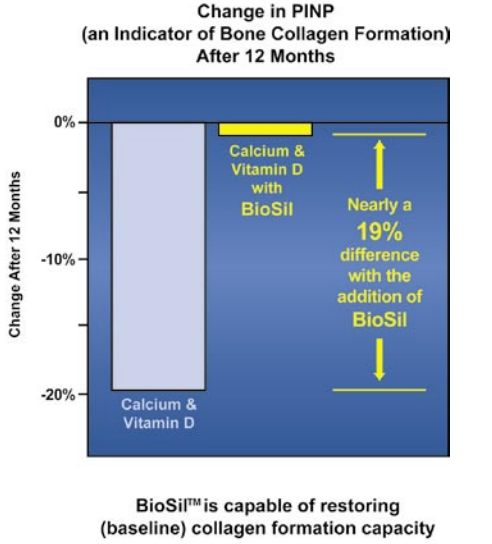


Based on Spector, et al.(2005) J Bone Miner Res, 20, S172.

the femur (thighbone) compared with women taking only calcium and vitamin D. Just as impressive were results for bone collagen synthesis. Procollagen Type I N-terminal Propeptide (PINP) is the most sensitive marker for bone collagen formation, hence also closely linked to the formation of bone. In the active arm, PINP demonstrated significant improvements after 12 months amongst volunteers in the BioSil groups. Researchers concluded, "this study suggests that combined therapy of ch-OSA plus Ca/Vit D3 is a safe, well tolerated treatment that has a potentially beneficial effect on bone turnover, especially bone collagen, and possibly femoral BMD, compared to Ca/Vit D3 alone."

These results seem to confirm the results of previously conducted studies on chickens and rats in which choline-stabilized orthosilicic acid also significantly increased the BMD of the femur (thigh bone). In fact, choline-stabilized orthosilicic acid partially prevented bone loss in the ovariectomized rat model, a standard model for postmenopausal osteoporosis. The Spector study indicates that a quite low dose of BioSil (supplying only 6 mg silicon per day) provides significant benefits with approximately 12 months of usage. Among other things, this shows a high degree of safety. ■

BioSil for Hair and Nails

Users of BioSil as a supplement often have reported an increase in the strength of their hair and nails. These two fast-growing cell-free tissues are composed predominantly of the structural protein keratin, which is organized into tight, highly-cross-linked fibers. Recently in a clinical trial published by Barel, et al. (2005), after 20 weeks of BioSil supplementation (10mg/day silicon), both hair and nail brittleness was significantly lower than in a control group. ■

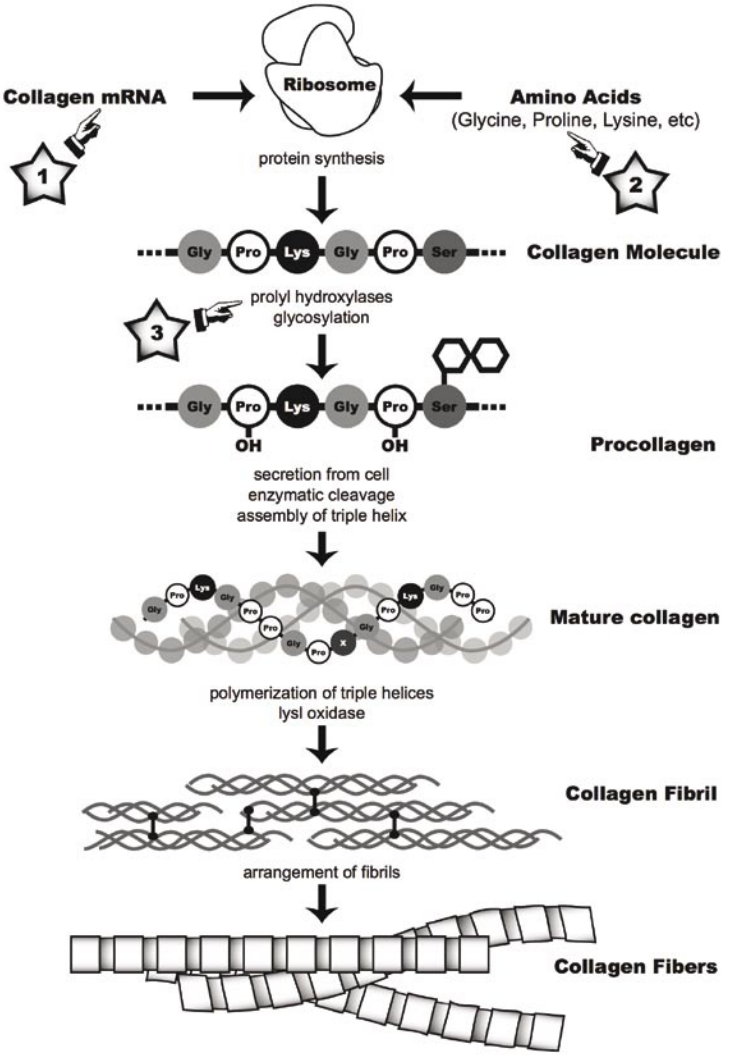
Building the Extracellular Matrix

Unlike the majority of trace elements in human nutrition, which perform a myriad of different functions, silicon has a singular role in human metabolism: it promotes the formation of extracellular matrix (ECM). The extracellular matrix is the complex network of proteins and carbohydrate polymers that forms the fundamental structure of our tissues and organs. The stability and proper function of the various systems of our body (bones, vasculature, skin) is dependent on the formation and maintenance of a healthy extracellular matrix.

The predominant building blocks for ECM are drawn from two classes of macromolecules, proteins and polysaccharides. Specifically, the major structural proteins of ECM are the collagens and elastin, and the major polysaccharides of the ECM are a class of nitrogen-containing poly sugars called glycosaminoglycans (GAGs). Collagens and elastin form fibers or membranes that function as the core of the ECM. GAGs augment the physical properties of this protein core, modifying its strength, elasticity, lubrication, or hydration in order to produce tissues of the desired mechanical parameters.

In collagen synthesis, silicon appears to function as a cofactor for enzymatic activity, stimulating both cellular protein synthesis machinery and the multi-step enzymatic conversion of immature collagen into its mature, biologically relevant form. The complex organization of individual collagen molecules into twisted bundles (fibrils), and their subsequent organization into fibers or membranes, is dependent on a series of critical reactions. These reactions occur both inside and outside of the cell, and require the activity of several enzymes, amino acids (glycine and proline), vitamin C, and trace elements (silicon, iron, copper).

A number of studies utilizing choline-stabilized orthosilicic acid have demonstrated a stimulatory effect on collagen synthesis and collagen content in bone, cartilage, and skin. There are at least three putative roles for silicon in collagen synthesis. First, it is required for prolyl hydroxylase activity. The prolyl hydroxylases add hydroxyl (OH) groups to specific proline residues in the procollagen; these hydroxyprolines can interact with one another between the individual chains though chemical bonding (hydrogen bonding). This adds strength between chains. Second, silicon has been postulated to have a



The Formation of Collagen mRNA and amino acids (particularly glycine and proline) are used by cellular machinery (ribosomes) to synthesize the collagen molecule. The collagen molecule is a repetitive triplet sequence of amino acids (circles) (Glycine-Proline-X, where X can be any of the 20 proteogenic amino acids). The activity of cellular prolyl hydroxylases attaches hydroxyls (-OH) to the prolines to form hydroxyprolines; sugars (hexagons) can also be attached to the collagen molecule. This new molecule, procollagen, is secreted from the cell. After procollagens are cut to length by extracellular proteases, three procollagen molecules together to form a triple helix (mature collagen). Mature collagen molecules polymerize together to form collagen fibrils, with crosslinks formed between lysines in each strand (black lines). Fibrils bundle together to form the fibers that build the extracellular matrix. Silicon (stars) has been shown to stimulate this process of collagen formation by (2) stimulating the synthesis of proline and (3) by stimulating the enzymatic activity of prolyl hydroxylases; more speculative is (1) the stimulation of collagen mRNA synthesis.

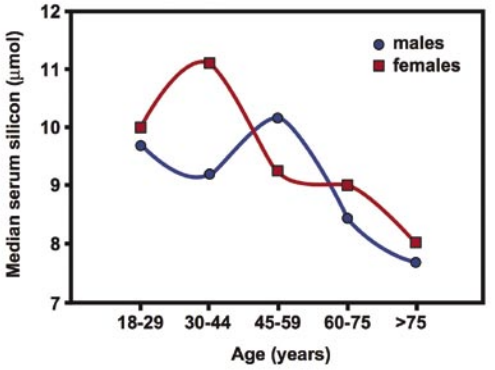
role in proline synthesis by stimulating the activity of a key enzyme in proline synthesis (liver ornithine aminotransferase). A decrease in proline synthesis has a deleterious effect on collagen production by limiting the availability of one of its key amino acid building blocks. Finally, silicon may increase the production of collagen mRNA, an indicator of, and requirement for, collagen synthesis. This last point remains somewhat speculative because one recent cell culture study employing physiologic concentrations of orthosilicic acid failed to find an increase in mRNA, only an effect on alkaline phosphatase and osteocalcin. Therefore, further research is needed to clarify this mode of action in humans, as opposed to test tube experiments. ■

Supplementing with BioSil

Were we to consume the foods our bodies evolved with, our diets should theoretically provide sufficient silicon and related factors for our needs. However, there are several reasons that supplementation with choline-stabilized orthosilicic acid may be desirable. For instance, our dietary habits have changed and our sources of food have changed from those of our ancestors. In general, we tend to eat less of the types of foods that supply large amounts of silicon (particularly fiber-rich, unprocessed grains) or co-factors, such as phytoestrogens, important for bone and general health. Processed food diets are unlikely to provide optimum silicon nutrition. Modern processing, while adding stability and convenience to our food sources, reduces their inherent silicon levels. Moreover, even when there are relatively good dietary sources of silicon, various animal experiments have demonstrated that adding choline-stabilized orthosilicic acid to the diet has significant health benefits.

In addition, our nutritional requirements appear to change with age. Serum silicon concentrations appear to be age dependent and to fall with advancing years. Bisse, et al. (2005) showed that there are dramatic decreases in silicon concentrations between the ages of 18 and 75. The process of aging can have a twofold effect on the decrease of dietary silicon: studies have shown that as people age they tend to consume more refined foods and less of the silicon-rich whole grains, raw fruits and vegetables. Also, the conversion of silica to orthosilicic acid becomes less efficient with age due to decreased production of stomach acid. Even were this not the case, experimental and clinical evidence has shown that supplemental silicon may have beneficial effects with otherwise silicon-rich diets. Only modest increases in elemental intake as choline-stabilized orthosilicic acid have been sufficient to produce positive effects (compare the 6–10 mg day dosages for the BMD and skin studies with the estimated 20–33 mg/day average dietary silicon intake). By providing optimal, and not simply sufficient levels of silicon in the diet, the accumulation of low levels of dysfunction may be circumvented, which may aid in the prevention of serious health consequences.

Orthosilicic or monosilicic acid (OSA) is one of the simplest silicon-containing molecules and serves as the basic silicon source for the majority biological reactions in higher animals.



Serum Silicon Concertration Decrease with Age

Requiring no chemical conversion before absorption, orthosilicic acid appears to be the most biologically available form of silicon and it has been the primary agent in most recent work in the area of silicon nutrition. Until late middle age, approximately half of ingested orthosilicic acid is absorbed, a figure consistent with the absorption of silicon from mineral-rich water. As a highly reactive molecule, orthosilicic acid can spontaneously polymerize into amorphous silica at physiological conditions (neutral pH), a fact that complicates its storage and handling. Stabilizing orthosilicic acid by the addition of a quaternary amino compound (such as choline) results in choline-stabilized orthosilicic acid, which is a concentrated source of orthosilicic acid with high bioavailability and a long shelf life. Moreover, the choline component is important for maintaining the structural integrity of cellular membranes; hence, it supports the benefits of orthosilicic acid supplementation. Current and on-going experiments with BioSil suggest that there are results found with supplementation with choline-stabilized orthosilicic acid that cannot be explained entirely on the basis of this compound being a source of biologically active silicon. ■

Conclusion: It's in the Collagen

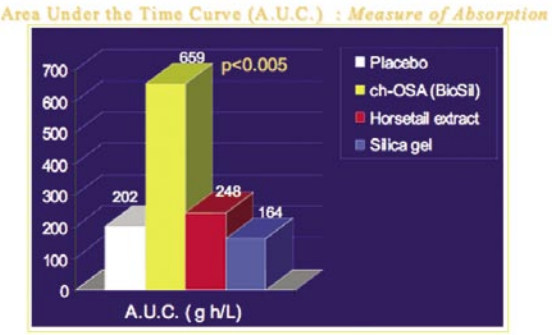
Choline-stabilized othosilicic acid has been a primary research tool over the last decade in studies examining how an oral supplement can improve the health of the skin and bones. Recent clinical trials have confirmed much earlier work using this compound. The benefit? It's in the collagen.

Collagen is an aspect of the extracellular matrix, the complex webbing that holds cells in their proper place. Collagen gives structure to the skin and acts as the scaffolding for the construction of new bone. When collagen and its precursor, procollagen, are reduced in the skin due to aging and photodamage, the tight, smooth

and resilient weave of the outer surface of the body becomes more rough and coarse. When procollagen and type I collagen decrease in bone, the scale is tipped from balance, stable BMD and good resilience towards mineral loss and less structural stability. Bone quantity and bone quality are both affected.

Choline-stabilized orthosilicic acid is a unique and patented compound that has been shown clinically to support skin and bone health. The supplement is safe, easy to take and highly researched. It is manufactured in Europe under stringent production standards and commercialized in the US under the brand name BioSil™. For skin care, one capsule daily supplying 5 mg of silicon in the form of choline-stabilized orthosilicic acid is sufficient; intensive care is two capsules per day. For bone health, two capsules daily of a synergistic formula supplying 6 mg of silicon in the form of choline-stabilized orthosilicic acid is suggested. Effects have been demonstrated with these very low dosages of silicon in this form.

With regard to both skin and bone health, it should be remembered that BioSil works by helping the body to renew the underlying structural components of these tissues. Benefits are clinically proven and long lasting, but they do not appear overnight. Improvements in skin health depend upon the turnover and replacement of the collagen support structure, a process that takes several months. Therefore, one should expect improvements in the skin to appear gradually over this period of time. Most individuals first notice benefits to hair and nails within six to eight weeks, and then benefits to the skin in three to six months. Support for bone health requires even longer-term supplementation, just as is true of supplementation with calcium and vitamin D. Clinical findings of significantly improved bone mineral density and improved procollagen production were demonstrated with twelve months of supplementation. This suggests that BioSil should be used daily along with calcium and vitamin D to maximize the benefits found with these nutrients. ■



In a human trial, equal amounts of silicon were provided as BioSil (ch-OSA), herbal silica (horsetail herb) and silica gel. The amount of silicon absorbed from these various sources was measured as the increase in blood serum silicon levels (Area Under the Time Curve). BioSil proved to be far more bioavailable than the alternatives tested. Based on Calomme, et al. (2000) Trace Elements in Man and Animals, 10, 111–4.

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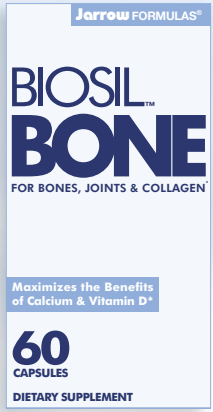

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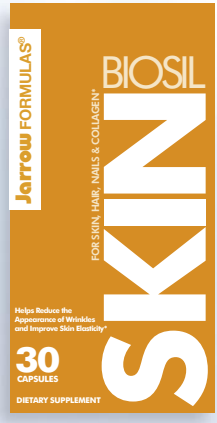

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