ch-OSA®
(choline-stabilized orthosilicic acid)

Clinically Proven

Reduces Fine Lines and Wrinkles – Increases Skin Elasticity - Thickens and Strengthens Hair – Strengthens Nails – Promotes Strong and Flexible Bones

ch-OSA® - What is it ?

ch-OSA® or *choline-stabilized orthosilicic acid* is a complex, clinically proven to activate the biological pathways that generate collagen.

Collagen is a fibrous protein, essential for the structural integrity and biomechanical properties of connective tissue and is present in high amounts in skin, bones and joints. Starting at age 21, collagen in skin decreases linearly with 1 % per year (Shuster et al. 2005) resulting in a decline of skin thickness (Brincat et al. 1987) and elasticity. Post-menopausal changes are even more dramatic with a loss of 30 % skin collagen in the first 5 years (Baumann et al. 2007) and an annual decline in skin elasticity of 0.55 % (Sumino et al. 2004). Elasticity is correlated with the depth of wrinkles, suggesting that the formation of wrinkles primarily results from the loss of elasticity (Akazaki et al. 2002). Importantly, the postmenopausal decrease in skin collagen correlates with the age-related decrease in bone mineral density (Sumino et al. 2004). ch-OSA® is a unique, patent protected complex with health benefits for hair, skin, nails and bone proven by randomized, double-blind, placebo-controlled clinical trials. The scientists who were involved in these trials explain ch-OSA's health benefits as the result of activating pathways which generate collagen.

ch-OSA® technology

Orthosilicic acid or OSA, is a natural compound present in very dilute concentrations in mineral water and beverages such as beer, however it loses its stability during bottling and processing.

A new technology has been developed to stabilize and concentrate OSA using choline, a GRAS approved nutrient. Choline-stabilization is the most advanced OSA stabilization technology known today. The positively charged nitrogen atom in choline interacts with electronegative oxygen in OSA, resulting in the formation of a specific complex. ch-OSA® is only formed when OSA is synthesized *de novo* in presence of choline. The ch-OSA® technology uses choline because it has been proven to be the "ideal" stabilizer of OSA. Not only does choline stabilize OSA but it also provides vital-health promoting benefits. Choline is a precursor of phospholipids which are essential to built cell membranes and is also involved in cell signaling (e.g. the neurotransmitter acetylcholine), lipid metabolism, protection against homocysteine mediated breakdown

of collagen, and it suppresses inflammation and oxidative stress (Blusztajn 1998; Metha et al. 2009, Zeisel et al. 2009). Beyond its ability to stabilize OSA, the choline component of ch-OSA® may bind to specific, cellular receptors for choline. As a result, ch-OSA® can enter target cells and activate biological pathways.

ch-OSA® is available as a liquid and in the form of encapsulated beadlets. The beadlets are produced by a novel, patent pending "extrusion-spheronization" technology used to bind microdroplets of ch-OSA® liquid on a microcrystalline cellulose carrier.

Clinical Evidence

The health benefits of ch-OSA® are proven in studies on humans performed at internationally renowned research institutes. All these studies are randomized, placebo-controlled, double blinded clinical trials, published in international, peer-reviewed medical journals. Supporting evidence is also found in published animal trials and in-vitro studies.

Skin, hair and nails

A first clinical trial was undertaken by the University of Brussels in Belgium (Barel et al. 2005) to evaluate the effect of ch-OSA® on photo-aged skin. Photo-ageing is the result of chronic exposure to ultraviolet radiation (e.g. sun, sunbeds) superimposed on chronobiological (intrinsic) ageing. Photo-aged skin is characterized by major changes in the dermis i.e. a marked decrease in collagen, glycosaminoglycans and proteoglycans combined with a degeneration of elastic fibers (elastosis) resulting in a rough leathery skin surface with many fine and coarse wrinkles. Typically, decreased elasticity is found in photo-aged skin as a result of the degraded mesh of collagen and elastine fibers in the dermis. Over time these changes also occur in normal, chronobiogical ageing, therefore photo-aging is considered to be a valuable model to study anti-ageing products. In the clinical trial, fifty (50) healthy women, aged between 40 and 65 years, with clear signs of photo-aging were randomized in a ch-OSA® and a placebo group. Participants were instructed not to change their daily dietary and cosmetic regimen during the course of the study. In addition, any dermatological or anti-aging therapy was prohibited. Non-invasive, validated methods were used to evaluate skin roughness (Visiometer skin replica) and mechanical anisotropy (Reviscometer). Quantifying skin microrelief is a standard method to measure the depth of fine lines and wrinkles and include typical parameters such as "maximum roughness" (Rm) i.e. the in depth of the main wrinkle. Mechanical anisotropy of skin is used as an indirect parameter of skin elasticity. The participants also scored the severity of hair and nail brittleness on a numeric scale. After 20 weeks, the depth of the main wrinkle improved significantly in the ch-OSA® group by 19 % but increased in the placebo group by 11 %, resulting in an overall improvement of 30 % (figure 1).

Skin microrelief in young skin is characterized by a multi-directional pattern of lines (figure 2). When skin ages the lines become both deeper and more oriented in a dominant, single direction. These changes in microrelief reflect the ongoing deterioration with age of the underlying collagen framework in the dermis. Women who took ch-OSA® were found to have after 20 weeks a more multidirectional pattern of skin lines compared to the start of the study (baseline), resembling "younger" skin as a result of a dense collagen framework in the dermis.

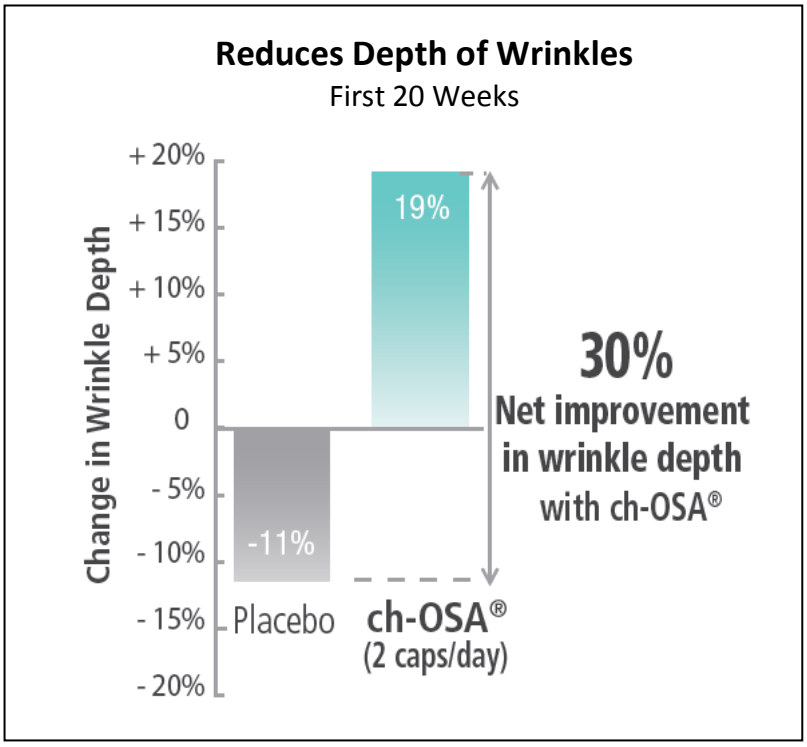

Figure 1: Change in "maximum roughness" (Rm) i.e. the change in depth of the main wrinkle in women with photo-aged skin who took for 20 weeks ch-OSA® or a placebo. The difference between both groups was statistically significant ($p<0.05$). (Barel et al. 2005).

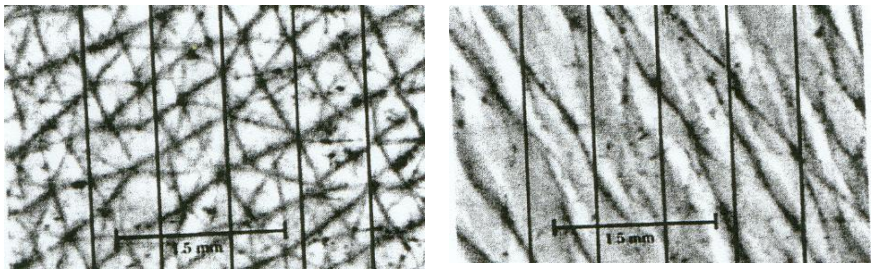

Figure 2. Skin microrelief of a 22 year (left) and 62 year (left) old women at the forearm. The microrelief in young skin has a typical multi-directional pattern of shallow lines whereas in older skin lines are oriented in dominant direction and become deeper. (De Paepe et al. 2007).

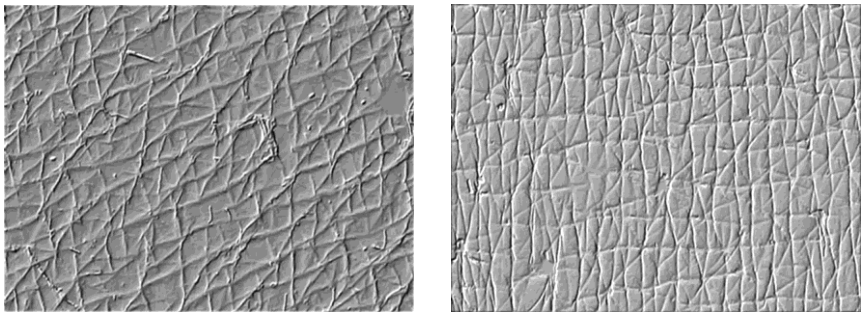

Figure 3. Skin microrelief of a participant in the clinical trial (Barel et al. 2005) at baseline (left) and after 20 weeks supplementation with ch-OSA® (right). A more multi-directional pattern of shallow lines resembling "younger" skin is observed compared to baseline as a result of a dense collagen network in the dermis. (Barel et al. 2005).

Skin elasticity, measured as mechanical anisotropy, increased significantly in the ch-OSA® group compared to the placebo group i.e. 89 % improvement was observed in the ch-OSA group over placebo. The investigators explained the reduction in fine lines and the improvement in skin elasticity as a regeneration or *de novo* synthesis of collagen fibers i.e. the activation of collagen pathways by ch-OSA® resulting in a dense collagen framework in the dermis and better skin quality. Supporting evidence is found in an animal study from the University of Antwerp, Belgium (Calomme et al. 1997). Young animals were given ch-OSA® or a placebo in their diet and randomly chosen skin biopsies were analyzed for the hydroxyproline content. Hydroxyproline is a specific component of collagen i.e. it can be used as a marker of collagen content. A significant 12.5 % higher hydroxyproline content was found in skin of animals on the ch-OSA® diet compared to skin of placebo controls.

In the study of Barel et al. (2005), the score for brittleness of hair and nails (figure 4) decreased significantly in the ch-OSA® group whereas no significant change was observed for women in the placebo group.

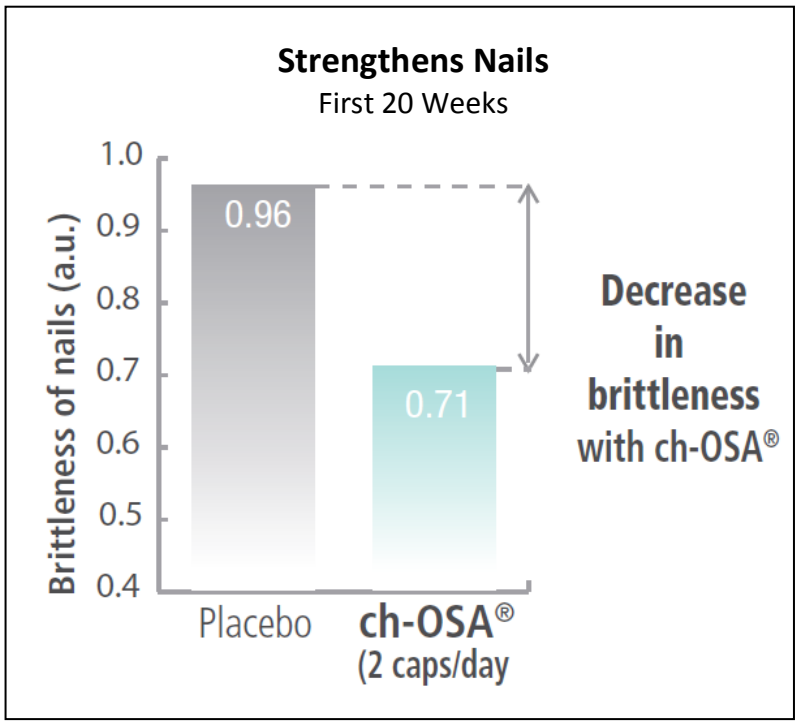

Figure 4: Brittleness of nails in women who took for 20 weeks ch-OSA® or a placebo. Brittleness was evaluated on a 4-point scale with "0" no brittle nails, "1" slight, "2" moderate, and "3" severe. After 20 weeks a significant decrease was observed in the ch-OSA group compared to baseline ($p<0.05$) but no change was found for women in the placebo group. (Barel et al. 2005).

The effect of ch-OSA® on hair quality was further investigated in a collaborative study led by professor Randy Wickett of the University of Cincinnati (Wickett et al. 2007). Forty-eight (48) women aged between 18 and 65 years, with fine hair were randomized in a ch-OSA® and a placebo group. Hair morphology and tensile properties were evaluated with validated methods. Tensile properties include the elasticity of the hair (elastic gradient) and the force needed to break hair fibers (break load). After 36 weeks the elasticity significantly decreased in the placebo group but remained unchanged in women who took ch-OSA®. The break load was found 13.1 % higher in women taking ch-OSA® compared to women in the placebo group. With respect to hair morphology, women who took for 36 weeks ch-OSA® had a 12.8 % bigger

cross-sectional area of hair fibers compared to women taking placebo. Several mechanisms of action were suggested by the investigators to explain these results. A direct interaction with keratin is possible considering that silanol groups in ch-OSA® form complexes with amino acids and peptides. Such an interaction could change the biomechanical properties of hair since keratin is the major constituent of hair. The increase in cross-sectional area suggests that ch-OSA® has a structural influence on keratin fibers or on the hair follicle. Since the hair follicle is embedded in a collagen rich matrix, stimulation of collagen synthesis by ch-OSA® will improve the flow of nutrients to the hair follicle resulting in more keratin formation. While most of the hair structure arises from epidermal keratinocytes, a specialized population of fibroblasts called the dermal papilla controls hair growth and hair volume. Increased collagen synthesis by ch-OSA® in fibroblasts of the dermal papilla, will increase the volume of the dermal papilla resulting in a bigger cross-sectional area of the newly formed hair shaft.

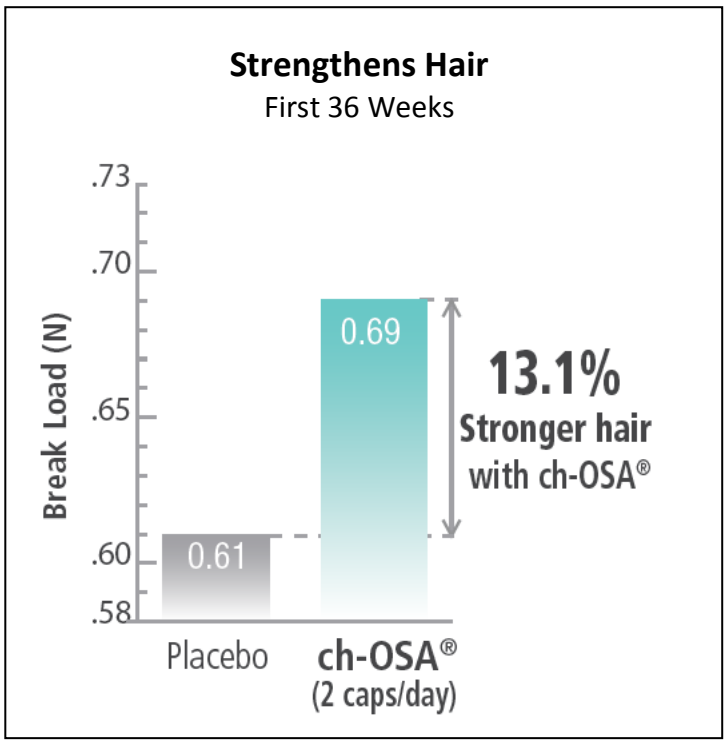

Figure 5: The “break load” of hair in women who took for 36 weeks ch-OSA® or a placebo. Break load is the force needed to break hair fibers. (Wickett et al. 2008).

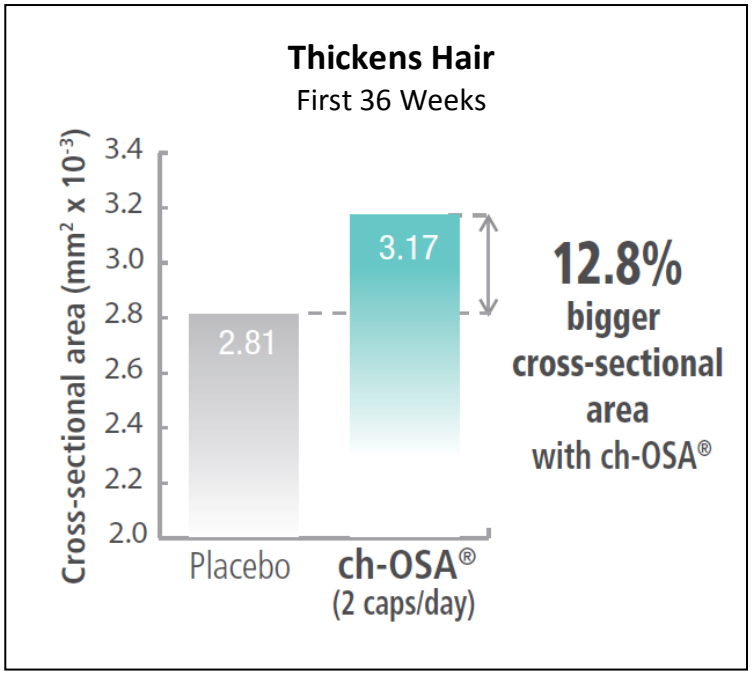

Figure 6: Hair morphology i.e. cross-sectional area of hair in women who took for 36 weeks ch-OSA® or a placebo. The cross-sectional area was significantly bigger in the ch-OSA group compared to to women in the placebo group ($p<0.05$). (Wickett et al. 2008).

Bone Health

The effect of the ch-OSA® on markers of bone turnover and bone mineral density was investigated in a clinical trial at the St Thomas Hospital in London led by professor Tim Spector (Spector et al. 2008). Hundred and eighty-four (184) osteopenic and osteoporotic, but otherwise healthy women with a T-score at the lumbar spine of < -1.5 were randomized in ch-OSA® and placebo groups. All the subjects took 1000 mg calcium and 20 mcg cholecalciferol daily. Biochemical markers of bone formation and bone resorption were measured and bone mineral density (BMD) was assessed by Dual-Energy X-Ray Absorptiometry.

Overall there was a trend for ch-OSA® to have a positive effect on bone formation markers. In particular, the procollagen marker PINP (procollagen type I N-terminal propeptide) increased significantly after 12 months in women who took ch-OSA® compared to women in the placebo group (figure 7). PINP is known as the most sensitive marker for bone collagen formation and an early marker of bone formation. Women on ch-OSA® who were osteopenic for both the lumbar spine and the hip were found to have a 2 % higher BMD at the critical hip region compared to women in the placebo group (figure 8). This difference in BMD was not only statistically significant but also clinically relevant since a 1 % differences with placebo is

generally accepted as the threshold for clinical relevance. A spokeswomen of the UK's National Osteoporosis Society, gave the following comment: *"We are especially interested in this work as it demonstrates potential benefits to people with osteoporosis. We are always supportive of advances in new therapeutic options."*

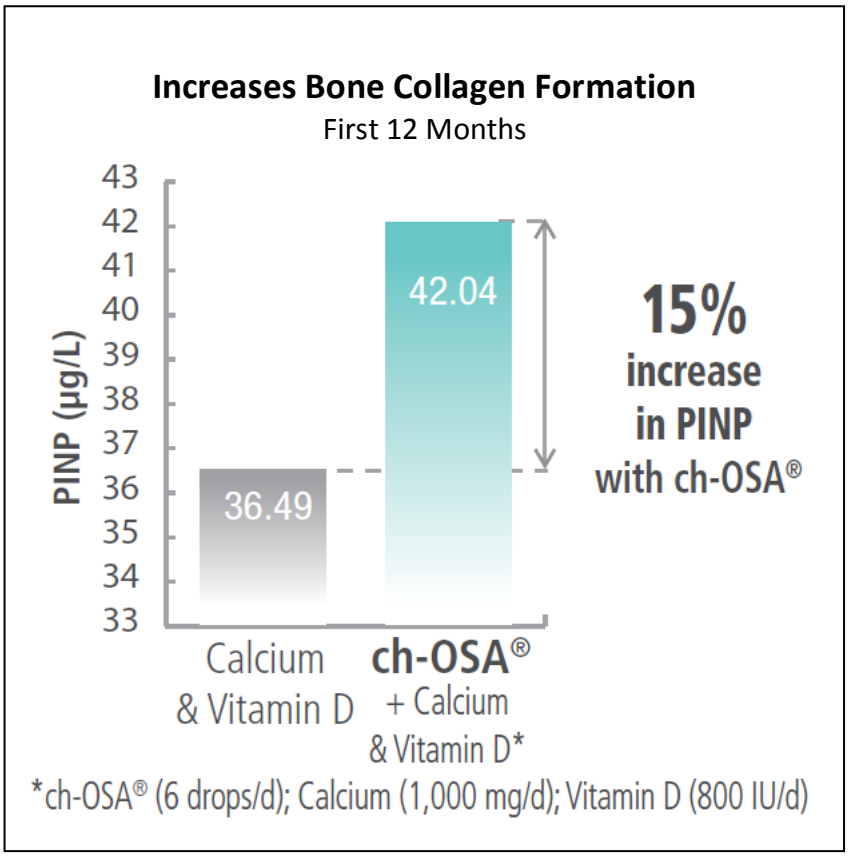

Figure 7: Bone collagen formation marker PINP (procollagen type I N-terminal propeptide) in osteopenic and osteoporotic women who took for 12 months ch-OSA® or a placebo. All women took also 1000 mg Ca and 800 IU of vitamin D daily. The difference between both groups was both statistically significant ($p<0.05$) and clinically relevant (i.e. a 10 % differences with placebo is generally accepted as the threshold for clinical relevance for a biochemical marker). (Spector et al. 2008).

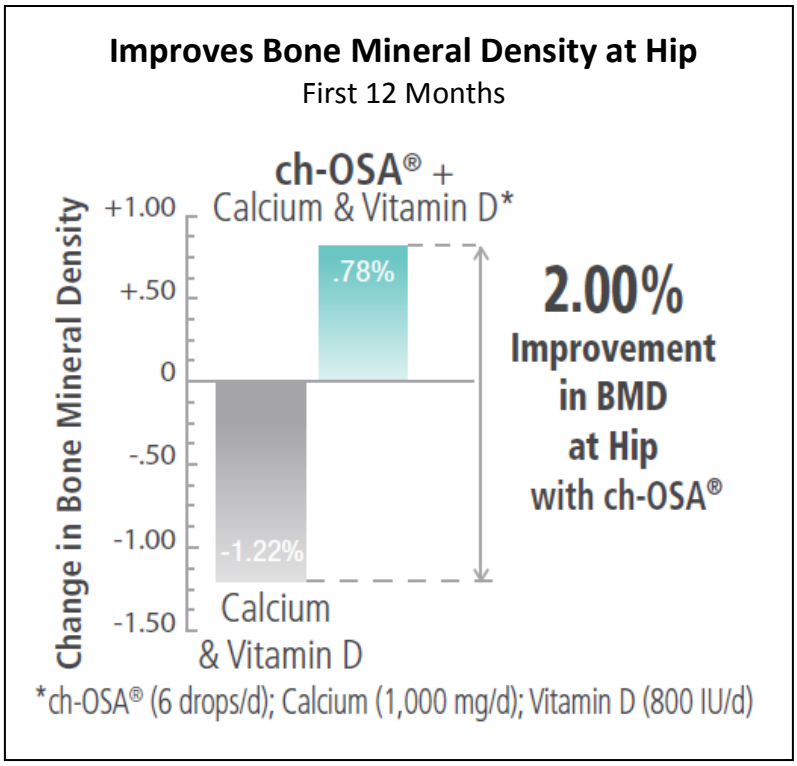

Figure 8: The change in bone mineral density (BMD) at the critical hip region in osteopenic women who took for 12 months ch-OSA® or a placebo. All women took also 1000 mg Ca and 800 IU of vitamin D daily. The difference between both groups was both statistically significant ($p<0.05$) and clinically relevant (i.e. a 1 % difference with placebo is generally accepted as the threshold for clinical relevance for BMD). (Spector et al. 2008).

Supporting evidence that ch-OSA® promotes bone health can be found in two animal studies. In an animal model for postmenopausal osteoporosis (Calomme et al. 2006) it was found that ch-OSA® increased the femoral BMD with 3 to 7 % in ovariectomized animals with a high bone turnover. Ovariectomy causes estrogen deficiency comparable to what happens in postmenopausal women. This condition will dramatically increase bone resorption and result in bone loss. This animal study demonstrates that ch-OSA® helps to prevent post-menopausal bone loss. In another experiment, it was shown in young, developing birds that ch-OSA® increased femoral BMD with almost 6 % and marginally improved the biomechanical properties of the femur (Calomme et al. 2002).

The fact that ch-OSA® increases bone collagen formation means that it can help improve bone quality. In fact, the soft framework of bone collagen fibers are essential for bone flexibility and fixation of calciumphosphate in the bone. This combination of collagen and calcium makes

bone both flexible and strong, which in turn helps bone to withstand stress (NIAMS 2009; Viguet-Carrin et al. 2006).

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