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ORIGINAL PAPER

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Abstract Chronic exposure of the skin to sunlight causes damage to the underlying connective tissue with a loss of elasticity and firmness. Silicon (Si) was suggested to have an important function in the formation and maintenance of connective tissue. Choline-stabilized orthosilicic acid (''ch-OSA'') is a bioavailable form of silicon which was found to increase the hydroxyproline concentration in the dermis of animals. The effect of ch-OSA on skin, nails and hair was investigated in a randomized, double blind, placebo-controlled study. Fifty women with photodamaged facial skin were administered orally during 20 weeks, 10 mg Si/day in the form of ch-OSA pellets ($n=25$) or a placebo ($n=25$). Noninvasive methods were used to evaluate skin microrelief (forearm), hydration (forearm) and mechanical anisotropy (forehead). Volunteers evaluated on a virtual analog scale (VAS, ''none = 0, severe = 3'') brittleness of hair and nails. The serum Si concentration was significantly higher after a 20-week supplementation in subjects with ch-OSA compared to the placebo group. Skin roughness parameters increased in the placebo group (Rt: +8%; Rm: +11%; Rz: +6%) but decreased in the ch-OSA group (Rt: −16%; Rm: −19%; Rz: −8%). The change in roughness from baseline was significantly different between ch-OSA and placebo groups for Rt and Rm. The difference in longitudinal and lateral shear propagation time increased after 20 weeks in the placebo group but decreased in the ch-OSA group suggesting improvement in isotropy of the skin. VAS scores for nail and hair brittleness were significantly lower after 20 weeks in the ch-OSA group compared to baseline scores. Oral intake of ch-OSA during the 20 weeks results in a significant positive effect on skin surface and skin mechanical properties, and on brittleness of hair and nails.

Keywords Photodamaged skin · Silicon · Orthosilicic acid · Nails · Hair

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Introduction

Healthy skin impedes the penetration of microorganisms which can cause infections and protects against irritants. Ageing leads to several changes in the skin and its appendages (hair, nails). These changes can be broadly categorized as either intrinsic ageing (chronobiological) or photoageing (actinic ageing). Intrinsic ageing results in subtle but important alterations of cutaneous function that are presumed to be due to time alone, whereas photoageing is the result of preventable chronic exposure to ultraviolet (UV) radiation superimposed on intrinsic ageing. Major changes of photoageing occur in the dermis. A marked decrease in collagen, glycosaminoglycans and proteoglycans is observed combined with a degeneration of elastic fibers (elastosis) resulting in a rough leathery skin surface with fine and coarse wrinkles. Furthermore, a loss of elasticity and an increase in mechanical anisotropy of the skin is observed. Premature ageing of the skin due to excessive exposure to UV light either from the sun or/and from sun benches is an increasing problem [32].

Silicon (Si) is a ubiquitous element present in various tissues in the human body [1] and is present in 1–10 parts per million in hair [29] and nails [1]. Studies of silicon deprivation in growing animals indicated growth retardation and marked defects of bone and connective tissue

[9]. Nutritional Si deficiency was found to decrease both the collagen synthesis and the formation of glycosaminoglycans in bone and cartilage [7]. In vitro, the activity of prolyl hydroxylase was reported to be dependent on the Si concentration in the medium of bone cultures, suggesting a Si-dependent pathway for collagen type I synthesis [8]. Others have suggested a structural role of Si in the cross-linking of glycosaminoglycans in connective tissue [25].

Recent animal studies confirm the involvement of Si in bone metabolism both in young animals [26, 27] and in models for postmenopausal osteoporosis [15, 24]. Subcutaneously implanted sponges of Si-deprived rats were found to contain less hydroxyproline compared to rats on a normal diet indicating that Si deprivation decreases collagen formation which is associated with wound healing [28]. In addition, the activity of liver ornithine aminotransferase, an important enzyme in the pathway of collagen formation, was lower in Si-deprived rats compared to Si-adequate rats [28].

Soluble Si is present as orthosilicic acid (OSA) in beverages and water. It is stable in dilute concentrations ($< 10^{-4}$ M) but polymerizes at higher concentrations around neutral pH into a range of silica species. Absorption studies indicated that only OSA is bioavailable, whereas its polymers are not absorbed [16]. Dietary silicates undergo hydrolysis, forming OSA which is readily absorbed in the gastrointestinal tract. Physiological concentrations of OSA stimulate skin fibroblasts to secrete collagen type I [23].

A stabilized form of OSA, choline-stabilized OSA (“ch-OSA”), was found to have a high bioavailability in humans compared to other Si supplements that contain polymerized forms of OSA [3, 33]. Supplementation of animals with low doses of ch-OSA resulted in a higher collagen concentration in the skin [5] and in an increased femoral bone density [4, 6].

Choline, the stabilizing agent in ch-OSA, is classified by the Food and Nutrition Board as an essential nutrient [12]. Although humans can synthesize it in small amounts, dietary sources are needed to maintain normal health [2]. Choline is important for the structural integrity of cellular membranes since it is the precursor of phospholipids (phosphatidylcholine and sphingomyelin) which are essential components of biological membranes. One of its metabolites, betaine, participates in the methylation of homocysteine to form methionine. Betaine is also known as an essential intracellular osmolyte [35]. Choline directly affects nerve signaling (as a precursor of the neurotransmitter acetylcholine), cell signaling (as a precursor for intracellular messengers such as diacylglycerol or ceramide, platelet-activating factor and sphingosylphosphorylcholine) and lipid transport/metabolism (required in the biosynthesis of very low-density lipoproteins).

In the present study we investigated the effect of oral intake of ch-OSA on skin, hair and nails in a randomized, placebo-controlled double-blind study in subjects with photo-aged facial skin.

Subjects and methods

Subjects

Fifty healthy Caucasian females, aged between 40 and 65 years, with clear clinical signs of photo-ageing of facial skin were included in this study after written informed consent. The subjects were assigned to two groups which were matched on the basis of photo type, age and actinic ageing. Subjects were randomly supplemented with ch-OSA or a placebo in each group. Women, using silicon supplements less than 3 months before the start of the trial or any food supplement other than the study medication during the trial, were excluded. In addition, subjects following any dermatological or cosmetical antiageing or antiwrinkle therapy including collagen, hyaluronic or botox injections, chemical and laser peelings, retinoic and alpha hydroxy acid treatment during the trial, were excluded. Furthermore, exposure to sun benches or sunlight was prohibited during the trial. The subjects provided a detailed list of all cosmetic products that they use daily. Subjects agreed not to change this daily regimen during the trial. On the day that noninvasive tests took place, subjects were instructed to refrain from using lotions, creams or other products on face and forearms. The trial was started in the autumn of 2003 and was completed in the spring of 2004.

Ethical approval was obtained from the regional Ethics Committee (Academic Hospital, Vrije Universiteit Brussel, Brussels, Belgium, protocol number 03/4 entitled antiageing effect of ch-OSA on photodamaged skin in healthy volunteers). The study was carried out in accordance to the Declaration of Helsinki (1964) changed by the 29th World Medical Assembly at Tokyo (1975).

Treatment

All patients were supplemented during 20 weeks with two capsules daily containing either the excipiens (microcrystalline cellulose pellets, Pharmatrans Sanaq AG, Switzerland) or 10 mg of silicon in the form of ch-OSA pellets (Bio Minerals n.v., Belgium). Subjects were instructed to take one capsule in the morning and another in the evening with a glass of water or juice. Placebo and ch-OSA capsules were identical in color, taste, odor and packaging and their content was blinded to the subjects and investigator.

Serology

Blood samples were collected from fasting subjects at baseline and after a 20-week supplementation, using Si-free polypropylene syringes (Sarstedt, Germany) and needles (Microlance, Becton Dickinson, Spain). Immediately after the sample was taken, the blood was

transferred into Si-free polypropylene tubes without anticoagulant (Sarstedt, Germany).

Si concentration in serum was analyzed in one batch by electrothermal atomic absorption spectrometry with inverse longitudinal Zeeman background correction (AAnalyst 800, Perkin Elmer, Bodenseewerk, Germany). Pyrolytic-coated graphite tubes were used. The hollow cathode lamp settings were respectively 30 mA lamp current, 251.6 nm spectral line and 0.2 nm band width. The injected sample volume was 20 µl and signals were measured in the peak-area mode. Serum samples were measured in duplicate by standard addition. Standards and serum dilutions were prepared in matrix modifier solution containing 72 mg/l $CaCl_2$ (Aldrich, Belgium), 1.508 g/l $NH_4H_2PO_4$ (Merck, Belgium) and 0.5 g/l Na_4EDTA (Aldrich, Belgium) in ultrapure water (conductance ≤ 0.08 μS). The sensitivity determined as the amount of silicon yielding a 0.0044 Abs.s signal was 90 pg. A pool of serum obtained from fasting healthy subjects was analyzed on several days to determine the inter-assay c.v. and was found to be 8.7% for a mean Si concentration of 109.09 µg/l ($n = 16$).

To evaluate the safety of oral treatment with ch-OSA, serum concentrations of urea, creatinine, uric acid, total protein, cholesterol, HDL-cholesterol, LDL-cholesterol and direct bilirubin, glutamic-oxalacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), gamma-glutamyltransferase (gamma-GT), cholinesterase, creatine kinase (CK), amylase and lipase were determined. Other parameters analyzed were sodium, calcium, phosphorus and zinc. All parameters were measured in serum at baseline and after 20 weeks of supplementation.

Noninvasive methods

All measurements were performed under standardized conditions, i.e., room temperature of 19 ± 2°C and a relative humidity level of 45–55%. An acclimatization time of at least 30 min was respected before measurements started. Hydration and microrelief of the skin were evaluated on the forearm, whereas visco-elastic properties were measured on the forehead, at baseline and after 20 weeks of supplementation, respectively, with the following noninvasive methods.

Hydration level of the skin surface was measured with the Corneometer CM 825 (Courage-Khazaka, Colgne, Germany) [10] and visco-elastic properties of the skin were measured with the Reviscometer MPA 5 (Courage-Khazaka, Colgne, Germany). The measuring principle of the Reviscometer is based on resonance running time. The time to propagate from transmitter to receiver is measured (shear wave propagation time) and is expressed in arbitrary units. This parameter is depending on the direction of the collagen fibers. Therefore, two measurements are made in a different angle, i.e., longitudinal vs lateral measurement. Mechanical anisotropy is an indicator of skin photoageing and was evaluated by the difference between longitudinal and lateral shear wave propagation time [14]. Microrelief (roughness) of the skin was measured with the skin visiometer SV 600 (Courage-Khazaka, Colgne, Germany). Investigated roughness parameters were Rt (depth of roughness), Rm (maximum roughness) and Rz (mean depth of roughness) [11].

Evaluation of hair and nail brittleness

Subjects were evaluated at baseline and after 20 weeks of supplementation; the degree of brittleness of hair and nails on a 4 point scale with "0" no brittle hair/nails, "1" slight, "2" moderate and "3" severe.

Statistical analysis

Differences between groups were evaluated with a Mann–Whitney U test and differences within groups were analyzed with a Wilcoxon-matched pairs signed rank test. $P < 0.05$ was considered to be significant.

Results

The mean age ($\pm$SD) in the placebo and the ch-OSA group was 49.2 ± 4.7 years and 51.8 ± 6.0 years, respectively. The mean body mass index was not significantly different between both groups (placebo: 24.1 ± 4.4, ch-OSA: 26.3 ± 5.7).

Mean baseline values of total cholesterol, LDL cholesterol and bilirubin were higher than the upper limit of the normal range in both the placebo and the ch-OSA group. All remaining parameters were within the normal range at baseline and after the 20-week supplementation in both groups. Twenty-four subjects in both the placebo and the ch-OSA group completed the study. In neither of the two treatment groups there were adverse effects reported that were related to the study medication.

The mean serum Si concentration was comparable for both groups at baseline but was significantly increased after 20 weeks of ch-OSA supplementation ($P < 0.0001$ vs T0 and $P = 0.0005$ vs 20 weeks placebo, Table 1), whereas no differences were observed in the placebo group.

Skin hydration decreased significantly after supplementation in both groups but no differences were found between the placebo and the ch-OSA group (Fig. 1).

Skin roughness parameters increased in the placebo group (Rt: +8%; Rm: +11%; Rz: +6%) but decreased in the ch-OSA group (Rt: −16%; Rm: −19%; Rz: −8%). The change in roughness from baseline was significantly different between ch-OSA and placebo groups for Rt (−0.12 vs +0.02 mm, $P < 0.05$) and Rm (−0.13 vs +0.05 mm, $P < 0.05$, Fig. 2).

The difference in longitudinal and lateral shear propagation time increased after 20 weeks in the placebo group but decreased in the ch-OSA group ($P < 0.05$, Fig. 3).

Table 1 Serum concentrations of silicon and safety parameters at baseline and after 20 weeks of supplementation (T20) with placebo and choline-stabilized orthosilicic acid (ch-OSA)

	Normal range		Placebo ($n=24$)		ch-OSA ($n=24$)	
	LL	UL	Baseline	T20	Baseline	T20
Urea(mol/l)		8.00	5.70 ± 1.10	5.30 ± 1.00	6.07 ± 1.15	6.17 ± 1.44
Creatinine(μmol/l)	53.00	123.00	77.83 ± 6.72	77.53 ± 8.05	81.36 ± 9.75	80.44 ± 7.52
Uric acid(μmol/l)	154.00	428.00	263.29 ± 62.61	236.02 ± 69.76	276.43 ± 72.26	253.12 ± 65.63
Total proteins(g/dl)			7.2 ± 0.3	7.3 ± 0.4	7.5 ± 0.3	7.4 ± 0.3
Cholesterol(mmol/l)		5.00	5.76 ± 0.83	5.55 ± 0.77	6.09 ± 1.27	5.85 ± 1.40
Triglycerides(mmol/l)		2.00	1.10 ± 0.55	0.87 ± 0.35	1.16 ± 0.67	1.07 ± 0.50
HDL cholesterol(mmol/l)	1.00		1.54 ± 0.30	1.55 ± 0.36	1.54 ± 0.26	1.51 ± 0.29
LDL cholesterol(mmol/l)		3.00	3.71 ± 0.75	3.60 ± 0.65	4.01 ± 1.17	3.85 ± 1.31
Bilirubin direct(μmol/l)		7.00	9.00 ± 2.18	8.96 ± 2.64	8.93 ± 2.84	8.08 ± 2.48
GOT(AST)(u/l)		37	22 ± 5	23 ± 5	22 ± 4	24 ± 6
GPT(ALT)(u/l)		38	8 ± 5	12 ± 5	9 ± 6	13 ± 8
Gamma-GT(u/l)		50	18 ± 10	17 ± 6	27 ± 19	24 ± 16
Cholinesterase(u/l)	3,930	11,500	6,847 ± 1427	6,812 ± 1261	7,311 ± 1376	7,286 ± 1510
CK(u/l)			87 ± 101	78 ± 43	77 ± 23	84 ± 46
Amylase(u/l)		96	49 ± 14	48 ± 11	48 ± 15	45 ± 14
Lipase(u/l)	7	60	23 ± 11	23 ± 12	22 ± 7	22 ± 10
Sodium(mmol/l)			136 ± 3	135 ± 3	137 ± 2	137 ± 2
Calcium(mg/l)	86	100	95 ± 4	96 ± 4	98 ± 3	97 ± 4
Phosphorous(mg/dl)	2,7	4.5	3.8 ± 0.4	3.8 ± 0.5	3.6 ± 0.4	3.7 ± 0.5
Zinc(μg/dl)	70	130	91 ± 14	85 ± 20	88 ± 10	89 ± 11
Silicon(μg/dl)			93.4 ± 74.7	97.6 ± 72.8	86.0 ± 53.9	168.8 ± 60.4[a,b]

LL, lower limit of normal range; UL, upper limit of normal range. HDL, high-density lipoproteins; LDL, low- density lipoproteins; GOT, glutamic-oxalacetic transaminase; GPT, glutamic-pyruvic transaminase; gamma-GT, gamma-glutamyl transferase; CK, creatine kinase. [a] $P<0.05$, vs baseline (Wilcoxon-matched pairs signed rank test); [b] $P<0.05$, vs T20 placebo (Mann–Whitney U test). Mean values ± SD are given. Serum silicon values were normally distributed.

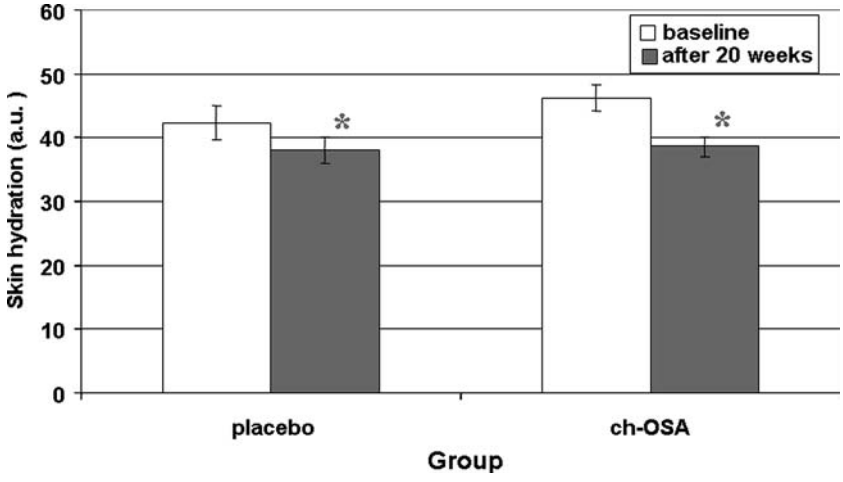

Fig. 1 Skin hydration (Corneometer CM 825) measured at the forearm at baseline and after 20 weeks of supplementation (T20) with placebo ($n=24$) and choline-stabilized orthosilicic acid (ch-OSA, $n=24$). * $P<0.05$ vs baseline, Wilcoxon-matched pairs signed rank test. Mean values ± SE are given

VAS scores for nail and hair brittleness were significantly lower after the 20-week supplementation with ch-OSA ($P<0.05$) compared to baseline scores (Fig. 4), whereas no significant differences were observed in the placebo group.

Discussion

Several studies have illustrated the beneficial effects of topical treatment with tretinoin [20] or alpha hydroxy acid [31] containing creams in cutaneous ageing.

Few studies investigating the effects of oral supplementation of minerals on aged skin have been published. Combined oral and topical treatment with colloidal silicic acid was found to have a positive effect on hair and nail brittleness in an open study [18]. However, no evidence was presented that the colloidal silica was absorbed in the gastrointestinal tract. In fact, polymerized forms of OSA such as colloidal silica are known to have a very low bioavailability compared to OSA [22]. Oral intake of extracts, derived from marine fish cartilage, was reported to have a repairing effect on photodamaged skin [19, 17]. However, it must be emphasized that

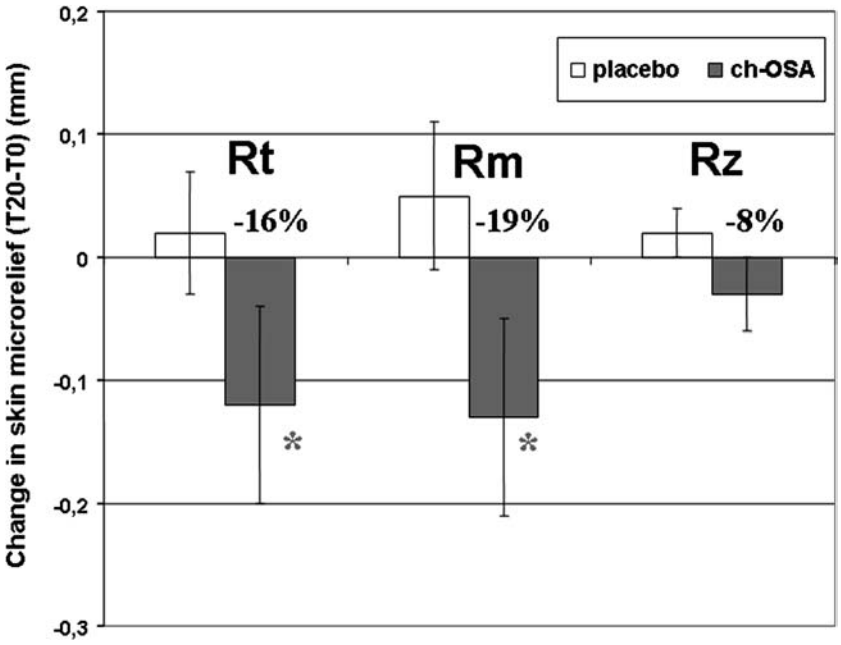

Fig. 2 Change in skin microrelief parameters (Visiometer SV 600) from baseline, measured at the forearm, after supplementation with placebo ($n = 24$) or ch-OSA ($n = 24$). Rt, depth of roughness; Rm, maximum roughness; Rz, mean depth of roughness. * $P < 0.05$ vs placebo, Mann–Whitney U test. Mean values ± SE are given

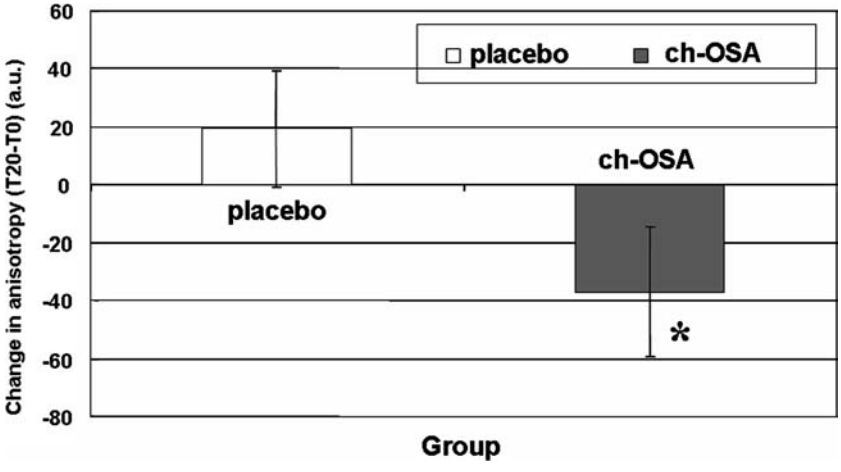

Fig. 3 Change in mechanical skin anisotropy (Reviscometer MPA 5) from baseline, measured at the forehead, after supplementation with placebo ($n = 24$) or ch-OSA ($n = 24$). Mechanical anisotropy was calculated as the difference between longitudinal and lateral shear propagation time. * $P < 0.05$ vs placebo, Mann–Whitney U test. Mean values ± SE are given

none of these studies were double blind nor placebo-controlled. Consequently, the obtained results could have been biased by seasonal influence and subjective evaluation.

The present study is the first randomized, double blind and placebo-controlled study that illustrates a positive effect of an oral supplement on skin microrelief and skin anisotropy in women with photoaged skin. The dose of ch-OSA supplementation (10 mg Si/day) was low compared to the average daily Si intake of 20–50 mg reported previously by Pennington [21]. The major dietary sources of Si are cereal/grain-based products and vegetables but modern food processing, including refining, is likely to reduce the dietary Si intake as it was shown that fibers contribute the most to the silicon content in plant-based foods [30]. After ch-OSA supplementation the serum silicon concentration increased with more than 90% compared to the baseline level which confirms the high bioavailability demonstrated in clinical [3, 33] and animal studies [5, 4]. In a comparative, bioavailability study [3], the silicon absorption from a single dose of ch-OSA (20 mg Si) was compared with colloidal silicic acid and phytolytic silica in healthy volunteers. Total silicon absorption was evaluated as the area under the time curve (AUC, serum Si concentration) and was found to be significantly higher for ch-OSA compared to the other silicon supplements and a placebo. In another study [33], the bioavailability of ch-OSA was compared with a silicon-rich diet and phytolytic silica. After a 4-day intake of ch-OSA (10 mg Si/day), both the serum Si concentration and the urinary Si excretion increased, whereas no increase was found after the intake of a Si-rich diet (45 mg Si/day, 31 days) and a normal diet (14 mg Si/day, 4 days).

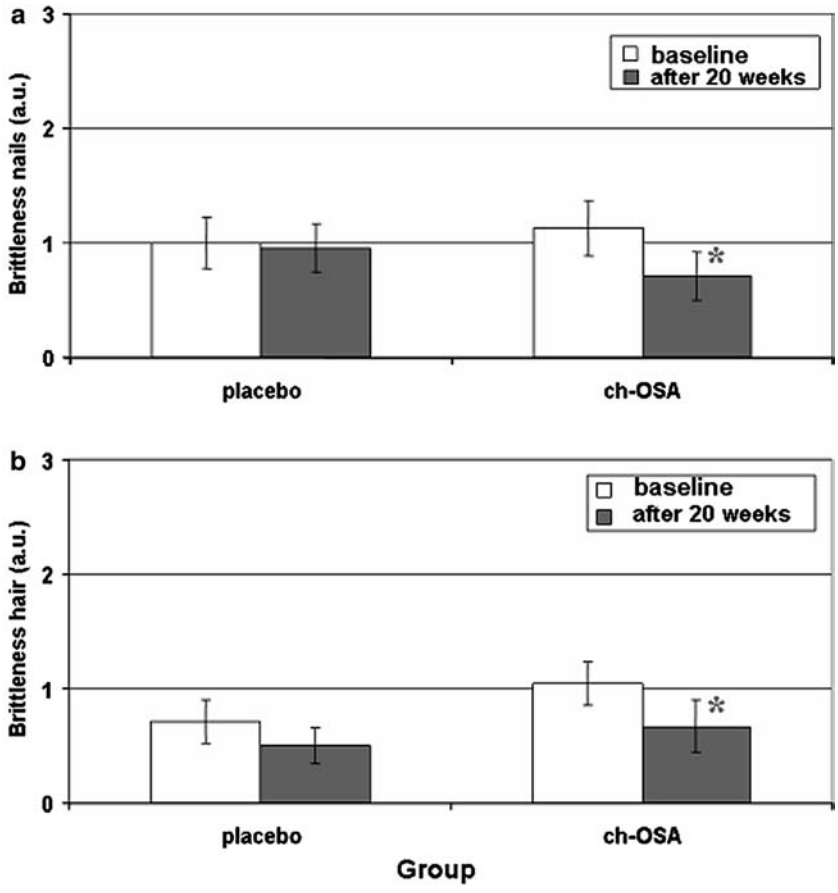

Fig. 4 Brittleness of hair and nails at baseline and after 20 weeks of supplementation (T20) with placebo ($n = 24$) and ch-OSA ($n = 24$). Brittleness was evaluated on a 4-point scale with "0" no brittle hair/nails, "1" slight, "2" moderate and "3" severe. Plot (**a**) nails; Plot (**b**) hair. * $P < 0.05$ vs baseline, Wilcoxon- matched pairs signed rank test. Mean values ± SE are given

The intake of 10 mg Si in the form of ch-OSA is safe as no adverse effects related to the study medication were reported. Serum safety parameters remained within the normal range. Total cholesterol, LDL cholesterol and bilirubin levels were already increased at baseline which is most likely due to the consumption of a diet high in cholesterol and saturated fats [13].

Both the ch-OSA group and the placebo group showed a small increase in hydration after 20 weeks of supplementation compared to baseline. Since all subjects started the study in October and finished the study in March, these changes are likely to be the result of a seasonal shift in temperature and relative humidity and are not related to the study medication. After 20 weeks of ch-OSA supplementation, both skin microrelief and mechanical properties improved. We previously demonstrated that oral intake of low doses of ch-OSA (5% increase of total dietary Si intake) during 24 weeks in calves resulted in a significant higher hydroxyproline content in the dermis compared to placebo and found a significant correlation between the serum Si concentration and the hydroxyproline content in cartilage [5]. Reffitt et al. found that low levels of OSA (typical serum concentrations) stimulate the synthesis of collagen type I in cultures of human osteoblasts and skin fibroblasts [23]. The OSA-dependent stimulation of collagen synthesis was abolished in the presence of prolyl hydroxylase inhibitors. As type I collagen and its monomer hydroxyproline are major constituents of skin, the improvement in skin parameters after ch-OSA supplementation points to potential regeneration or de novo synthesis of collagen fibers. Silicon was also reported to be involved in the synthesis of glycosaminoglycans [25] and was suggested to have a structural role as a cross-linking agent in connective tissue. Accordingly, treatment with ch-OSA might improve the glycosaminoglycan structure in the dermis and the keratin structure in hair and nails. Furthermore, the choline compound present in ch-OSA might have a synergistic effect with OSA since it is well known that choline is involved in several basic biological processes [2] including the fact that choline is a precursor of phospholipids such as phosphatidyl choline which is an essential component of cellular membranes. The physiological significance of choline is substantiated by the fact that intentional deprivation of choline disrupts cell growth and division [34].

To our knowledge, the present study is the first randomized, double blind placebo-controlled trial that illustrates the positive effect of an oral mineral supplement on skin surface and mechanical properties and on hair and nails brittleness, respectively.

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References

1. Austin JH (1977) Silicon levels in human tissues. Nobel Symp 255–268
2. Blusztajn JK (1998) Choline, a vital amine. Science 281(5378):794–795
3. Calomme M, Cos P, D'Haese P, Vingerhoets R, Lamberts L, De Broe M, Van Hoorebeke C, Vanden Berghe D (2000) Silicon absorption from stabilized orthosilicic acid and other supplements in healthy subjects. In: Roussel et al (eds) Trace elements in man and animals, vol. 10. Plenum, New York, pp 1111–1114
4. Calomme M, Sindambiwe J, Cos P, Vyncke C, Geusens P, Vanden Berghe D (2004) Effect of choline stabilized orthosilicic acid on bone density in ovariectomized rats. J Bone Miner Res 19:S449
5. Calomme MR, Vanden Berghe D (1997) Supplementation of calves with stabilized orthosilicic acid. Effect on the Si, Ca, Mg, and P concentrations in serum and the collagen concentration in skin and cartilage. Biol Trace Elem 56:153–165
6. Calomme MR, Wijnen P, Sindambiwe JB, Cos P, Mertens J, Geusens P, Vanden Berghe A (2002) Effect of choline stabilized orthosilicic acid on bone density in chicks. Calcif Tissue Int 70:292
7. Carlisle EM (1972) Silicon: an essential element for the chick. Science 178:619–621
8. Carlisle EM (1981) A silicon requirement for prolyl hydroxylase activity. Fed Proc 40:866
9. Carlisle EM (1981) Silicon: a requirement in bone formation independent of vitamin D1. Calcif Tissue Int 33:27–34
10. Clarys P, Barel AO, Gabard B (1999) Non-invasive electrical measurements for the evaluation of the hydration state of the skin: comparison between three commercial instruments- the Corneometer, the Skicon and the Nova DPM. Skin Res Technol 5:14–20
11. De Paepe K, Lagarde JM, Gall Y, Roseeuw D, Rogiers V (2000) Microrelief of the skin using a light transmission method. Arch Dermatol Res 292:500–510
12. Food and Nutrition Board (1998) Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, panthothenic acid, biotin, and choline. Institute of Medicine, National Academy Press, Washington, DC
13. Gaziano J et al (1996) Diet and heart disease. The role of fat, alcohol, and antioxidants. Cardiol Clin 14(1):69–83
14. Hermanns-Lê T, Jonlet F, Scheen A, Piérard GE (2001) Age and body mass index-related changes in cutaneous shear wave velocity. Exp Gerontol 36:363–372
15. Hott M, de Pollak C, Modrowski D, Marie PJ (1993) Short term effects of organic Silicon on trabecular bone in mature ovariectomised rats. Calcif Tissue Int 53:174–179
16. Jugdaohsingh R, Reffitt D, Oldham C, Davy JP, Fifield LK, Thompson RPH, Powell JJ (2000) Oligomeric but not monomeric silica prevents aluminum absorption in humans. Am J Clin Nutr 71:944–949
17. Kieffer ME, Efsen J (1998) Imedeen in the treatment of photoaged skin: an efficacy and safety trial over 12 months. J Eur Acad Dermatol Venereol 11(2):129–136
18. Lassus A (1993) Colloidal silicic acid for oral and topical treatment of aged skin, fragile hair and brittle nails in females. J Int Med Res 21:209–215
19. Murad H, Tabibian MP (2001) The effect of an oral supplement containing glucosamine, amino acids, minerals, and antioxidants on cutaneous aging: a preliminary study. J Dermatol Treat 12:47–51
20. Olsen EA, Katz HI, Levine N, Nigra TP, Pochi PE, Savin RC, Shupack J, Weinstein GD, Lufrano L, Perry BH (1997) Tretinoin emollient cream for photodamaged skin: results of 48-week, multicenter, double-blind studies. J Am Acad Dermatol 37:217–226
21. Pennington JA (1991) Silicon in food and diets. Food Addit Contam 8:97–118
22. Reffitt DM, Jugdaohsingh R, Thompson RP, Powell JJ (1999) Silicic acid: its gastrointestinal uptake and urinary excretion in man and effects on aluminium excretion. J Inorg Biochem 76:141–147
23. Reffitt DM, Ogston N, Jugdaohsingh R, Cheung HFJ, Evans BAJ, Thompson RPH, Powell JJ, Hampson GN (2003) Orthosilicic acid (OSA) stimulates collagen type 1 synthesis and osteoblast differentation in human osteoblast-like cells in vitro. Bone 32:127–135
24. Rico H, Gallego-Lago JL, Hernandez ER, Villa LF, Sanchez-Atrio A, Seco C, Gervas JJ. (2000) Effect of silicon supplement on osteopenia induced by ovariectomy in rats. Calcif Tissue Int 66:53–55
25. Schwarz K (1973) A bound form of silicon in glycosaminoglycans and polyuronides. Proc Natl Acad Sci USA 70(5):1608–1612
26. Seaborn CD, Nielsen FH (1994) Dietary silicon affects acid and alkaline phosphatase and ^{45} calcium uptake in bone of rats. J Trace Elem Exp Med 7:11–18
27. Seaborn CD, Nielsen FH (2002) Dietary silicon and arginine affect mineral element composition of rat femur and vetrebra. Biol Trace Elem Res 89:239–250
28. Seaborn CD, Nielsen FH (2002) Silicon deprivation decreases collagen formation in wounds and bone, and ornithine transaminase enzyme activity in liver. Biol Trace Elem Res 89(3):251–261
29. Smith BL (1993) Analysis of hair element levels by age, sex, race, and hair color. In: Anke M, Meissner D, Mills CF (eds) Trace elements in man and animals, TEMA 8. Kluwer Academic, New York, pp 1091–1093
30. Sripanyakorn S et al (2004) The silicon content of beer and its bioavailability in healthy volunteers. Br J Nutr 91:403–409
31. Stiller MJ, Bartolone J, Stern R, Smith S, Kollias N, Gillies R, Drake (1996) Topical 8% glycolic acid and 8% L-Lactic acid creams for the treatment of photodamaged skin. A double-blind vehicle controlled clinical trial. Arch Dermatol 132: 631–636
32. Trautinger F (2001) Mechanisms of photodamage of the skin and its functional consequences for skin ageing. Clin Exp Dermatol 26:573–577
33. Van Dyck K, Van Cauwenberghe R, Robberecht H, Deelstra H (1999) Bioavailability of silicon from food and food supplements. Fresenius J Anal Chem 363:541–544
34. Zeisel SH (1990) Choline deficiency. J Nutr Biochem 1:332–349
35. Zeisel SH (2003) Concentrations of choline-containing compounds and betaine in common foods. J Nutr 133:1302–1307