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Anti-Aging Effects of Monomethylsilanetriol and Maltodextrin-Stabilized Orthosilicic Acid on Nails, Skin and Hair

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Abstract: Chemical form of silicon determines its absorption and bioavailability: particulate and polymerized forms exhibit minimal oral bioavailability, while monomers (maltodextrin-stabilized orthosilicic acid, M-OSA) and organic compounds (monomethylsilanetriol, MMST) may hypothetically be highly absorbed. This study aimed to investigate the dermatological effects of oral ingestion of silicon, either solid (M-OSA–SiliciuMax® Powder) or liquid (MMST, SiliciuMax® Liquid) on the skin, hair and nails of healthy volunteers, through a clinical trial (Registry number 2,032,724. Full protocol at Plataforma Brasil website). Patients were randomized to receive 5 mg of elemental Si, either M-OSA or MMST (group 1 and 2, $n = 17$ each) or placebo (group 3, $n = 17$) twice a day for 150 days. Clinical and patients' subjective evaluations were conducted. Multispectral face imaging and hair mineral analysis were also performed. Use of M-OSA and MMST provided significant ($p < 0.05$) betterment of facial wrinkles and UV spots. Changes were also observed at the end of the study in skin texture and length of eyelashes. Hair aluminum levels decrease with the treatments. Self-reported questionnaire indicated good satisfaction with both M-OSA and MMST. Continuous use of both M-OSA and MMST can provide improvements on skin parameters, as well as act as a detox agent for aluminum.

Keywords: orthosilicic acid; monomethylsilanetriol; aging; nail care; skin care; hair care

1. Introduction

Silicon (Si) is ubiquitous in nature and constitutes the second most abundant element in the Earth's crust; in the human body, it is the third most abundant trace element [1,2]. However it is not normally found in free form in nature, occurring mainly complexed with oxygen and/or other elements (halogens, aluminum), forming crystalline silica (SiO_2, quartz), amorphous silica ($SiO_2 \cdot nH_2O$, opal) and silicates (kaolin, talc, feldspars, asbestos, clays, mica) [3]. In addition, this element is present in tissues of all living organisms. In particular, its higher concentrations in the human body can be found in the skin, as well as mucous membranes and connective tissues [4].

Although it is not yet formally recognized as an essential mineral, its importance in human nutrition and aesthetics has been cumulatively evidenced for decades. There is evidence that the body

levels of this element tend to decrease after the age of 30, and this process is more pronounced in postmenopausal stages for women [5].

Considering its major deposits in the body, this progressive reduction of Si throughout the years can be of sheer importance for dermatology. Data from the literature show that this decrease can affect the synthesis of collagen by the fibroblasts, as well as the activations of dermal collagenase—in this sense, improvement in collagen type I synthesis are one of the alleged benefits of Si supplementation [6]. Additionally, other benefits found in literature are: (i) promotion of the synthesis of elastin; (ii) stimulus for nail hardness; (iii) increase of resistance and thickness of hair fiber; and (iv) preservation of blood vessel elasticity [6–11]. These effects are important because skin ageing involves decrease in collagen, glycosaminoglycans and proteoglycans, together with degeneration of elastic fibers [6]. Deprivation of Si was also shown to affect the synthesis of glycosaminoglycans in bone and cartilage [12].

Although the eminent benefits of Si, it is important to take into account its chemical form during oral administration, as it determines its absorption and bioavailability. Si occurs naturally mainly as silicon dioxide (SiO_2) or as silicic acids derived from the hydration of this oxide, while orthosilicic acid [$Si(OH)_4$] is the simplest and the major chemical form of water soluble Si (and it is found mainly in beverages) [13]. In addition, the presence of the orthosilicic acid is known as the biological form of silicon in humans and animals and plays a major role in the release of silicon into living cells [2,4,14–16]. Despite the fact that Si is mainly absorbed from our diet as orthosilicic acid, when present in higher concentrations (it is stable only in concentrations lower than 10^{-4} M $\cong$ 10 mg/L) and with no addition of stabilizers to prevent self-association, this form of silicon polymerizes and forms silica (SiO_2) which allows very limited bioavailability (absorption ranging from 1% to 20%) [17]. Therefore, only monomeric orthosilicic acid and its small oligomers are soluble and can efficiently cross the intestinal barrier providing greater bioavailability.

In this search for a stable, high bioavailable form of Si, a number of molecules have been developed. Barel et al. [6] evaluated the oral intake of orthosilicic acid stabilized by choline during 20 weeks, and the results showed a significant positive effect on surface and mechanical properties of skin, and on brittleness of hair and nails. Kalil et al. [18] for their turn, reported recently the effects of orthosilicic acid stabilized by hydrolyzed marine collagen in a daily dose of 600 mg in a small population; they found positive results in skin rejuvenation in terms of firmness, hydration, and skin texture.

In this study, we focused on two different forms of Si: orthosilicic acid stabilized by maltodextrin (M-OSA) and monomethylsilanetriol (MMST). M-OSA is a new orthosilicic acid formulation stabilized by a hydrolyzed maltodextrin complex. Maltodextrin would act as a natural molecular support, complexing orthosilicic acid, increasing its stability as well as resulting in a final product with the presence of monomeric OSA and its small soluble and bioavailable oligomers. MMST is available as diluted solution and contain only unpolymerized forms of MMST (monomers and oligomers). MMST is an amphiphilic, and highly permeable organosilicon molecule [$Si(OH)_3CH_3$] that shows stability even at concentrations above 20 mM at room temperature and possesses rapid/high absorption and no adverse effects have been reported [16,17]. After its intestinal absorption, MMST is converted into biologically active orthosilicic acid [17].

In this sense, we investigated the oral intake of these two forms of Si (M-OSA and MMST) and their effects on nails, skin and hair through a randomized, placebo-controlled double-blind study in human subjects.

2. Materials and Methods

2.1. Study Setting and Population

This was a randomized, double-blind, placebo-controlled trial in healthy subjects. The study involved 51 women, ranging in age from 40 to 60 years (M = 49.6, $\pm$6.4, normal distribution according to Shapiro-Wilk test), and with phototypes described in Table 1. They were divided into three groups (*n* = 17 per group; allocation rate = 1:1:1): (G1) control (placebo: capsules containing maltodextrin);

(G2) treated with M-OSA (SiliciuMax® Capsules, Fagron, São Paulo, Brazil) containing 5 mg of elemental silicon every 12 h; (G3) treated with MMST (SiliciuMax® Liquid, Fagron, São Paulo, Brazil) (1 dosing cup containing 5 mg of elemental silicon every 12 h). Treatments were to be taken 15 min before breakfast and then 12 h after. The duration of the intervention was five months, with analyzes at baseline (T0), 3 months (T3) and 5 months (T5) after the beginning of the treatment.

Table 1. Baseline characteristics of the groups.

Characteristic	G1	G2	G3
Age (M ± SD)	48.5 ± 5.1	52.8 ± 5.9	47.6 ± 7.1
Phototype (*n*, %)			
III	8, 47.0	5, 29.4	7, 41.2
IV	8, 47.0	11, 64.7	8, 47.0
V	1, 6.0	1, 5.9	2, 11.8
Photodamage (*n*, %)			
Light	9, 52.9	1, 5.9	7, 41.2
Moderate	7, 41.2	15, 88.2	9, 52.9
Severe	1, 5.9	1, 5.9	1, 5.9
Skin oiliness (*n*, %)			
Dry	2, 11.8	1, 5.9	0, 0.0
Normal	9, 52.9	10, 58.8	10, 58.8
Oily	6, 35.3	6, 35.3	7, 41.2
Wrinkles (*n*, %)			
Fine	4, 23.6	2, 11.8	6, 35.3
Medium	10, 58.8	7, 41.2	6, 35.3
Deep	3, 17.6	8, 47.0	5, 29.4
Presence of spots (*n*, %)	17, 100.0	17, 100.0	17, 100.0

M = mean. SD = standard deviation. G1 = control (placebo). G2 = treated with maltodextrin-stabilized ortoshilic acid. G3 = treated with monomethylsilanetriol.

Before treatment, each patient undergone a clinical examination with the dermatologist to evaluate the general state of health and to verify suitability to the study. Eligibility criteria were: women considered healthy after clinical examination and who did not use any mineral supplementation during the study neither would perform any aesthetic procedure throughout the study. Exclusion criteria were: women not considered healthy after clinical examination; women using mineral supplements; women who have allergy/intolerance to silicon or any component of the supplements; women who were not willing to join the use of the supplement for the study period (5 months); women who had used silicon for at least three months prior to the start of the study; women following dermatological or cosmetic treatment or anti-wrinkle therapy including injections of collagen, hyaluronic acid and botulinum toxin botox, chemical or laser peels, or treatment with retinoic acid or hydroxy acids. Patients who have deliberately exposed themselves to the sun at critical times (10 a.m. to 4 p.m.) for tanning were withdrawn from the study. All procedures were conducted at the Federal University of Juiz de Fora. Patients and the dermatologist were blinded throughout the whole study. A pharmacist (H.C.P.) generated the random sequence and enrolled the participants. The random allocation sequence was computer generated: a list of continuous study numbers was generated with a random allocation to treatment 1 or 2 or 3. Study numbers were consecutive and given to patients by the staff at inclusion. The dermatologist explained the trial to the patient and obtained the patient's consent, as well as conducted the clinical examination. Staff gave the treatments according to sequence number, with no mention of the groups on the label.

2.2. Clinical Evaluation at Baseline

Clinical evaluation of the skin was performed by a blinded dermatologist, who determined Fitzpatrick skin type and evaluated sun damage (1—not present; 2—light; 3—moderate; 4—severe), oiliness (1—dry skin; 2—normal skin; 3—oily skin), wrinkles (1—fine; 2—medium; 3—deep) and spots (1—present; 2—absent).

2.3. Transonychial Water-Loss Evaluation

Water-loss on hand and foot nails were determined on a Vapometer (Delfin Technologies, Kuopio, Finland) at T0, T3 and T5. The equipment calculated the evaporation rate from the nails from the increase of relative humidity in the measurement chamber.

2.4. Skin Multispectral Imaging Evaluation

Baseline photos were taken of each patient, and an initial analysis was conducted with the Visia complexion analysis system (Canfield Imaging Systems, Fairfield, NJ, USA). Each patient was placed with the chin resting on the support of the equipment and the photos were taken from three angles: frontal, left hemiface and right hemiface. The parameters evaluated were: spots, pores, wrinkles, texture, porphyrins, UV spots, red areas, brown spots, volume and length of eyelashes and TruSkin Age® (Fairfield, NJ, USA) (a parameter calculated by the software which determines the patient's overall skin condition and age). Follow-up images were taken at T3 and T5 with the patient at the exact same position as in baseline.

2.5. Hair Mineral Analysis

250 mg hair samples collected at baseline and T5 next to the scalp (approximately 4 cm) were submitted to mineral analysis by inductively coupled plasma mass spectrometry (ICP-MS) in an 7700x spectrometer (Agilent, Tokyo, Japan). Samples were washed Triton X-100 detergent 1:200 aqueous solution in ultrasonic bath for 5 min and then rinsed with Milli-Q water. This procedure was repeat three more times and then the samples were rinsed with high-purity acetone, filtered, rinsed twice with Milli-Q water, rinsed twice with high-purity acetone and then let to rest in a Class II biological safety cabinet until completely dry. The dry sample was digested in closed-vessels with 2.5 mL of Suprapur® (Merck, Darmstadt, Germany) nitric acid 65% and 1 mL of Suprapur® hydrogen peroxide 30% at 70 °C until completely dissolved. The remaining liquid was then diluted to 25 mL with Milli-Q water and then injected into the nebulizer of the spectrometer by a peristaltic pump. Analyses were conducted under an argon plasma flux of 15 mL/min at 26.00 MHz with 40 s of sample uptake at 0.3 rps and using a helium collision cell to selectively attenuate all polyatomic interferences based on their size.

Standard curves were used to quantify the following elements: Si, Ca, Mg, Na, K, Cu, Mn Cr, V, Mo, B, Li, P, Se, Sr, S, Co, Fe, Ge, Rb, W, Al, Sb, As, Ba, Be, Bi, Cd, Pd, Hg, Tl, Ag, Ni, Sn, Ti, Te and Zr.

2.6. Subjective Evaluation

A structured self-reported questionnaire answered by each patient at T3 and T5 was used to patient's satisfaction with the treatment. Patients were requested to give a rate from 1 to 10 concerning the possible improvements in the following parameters: skin (hydration; homogeneity of skin tone; number of darkened areas; color intensity of darkened areas; wrinkles/lines of expression in the region of the lips; wrinkles/express lines in the forehead; wrinkles/expression lines in the eye region; general appearance; softness; signs of aging; lightness/luminosity; bleaching effect; bleaching speed; uniformization of skin imperfections; oiliness; desquamation; acne), hair (general appearance; hydration; nutrition; softness; vitality; aging signs; lightness; oiliness; dandruff) and nails (general appearance; resistance; growth; yellowing; stains; texture).

2.7. Statistical Analysis

First, in order to evaluate the homogeneity of the sample, the three groups were compared in the pre-test (T0), through Analysis of Variance (ANOVA One-Way) followed by Bonferroni Post Hoc Test. Afterwards, ANOVA was performed for repeated measurements (transonychial water-loss, skin multispectral imaging evaluation, and subjective evaluation). In all of these analyzes, the variable "Group" was considered as an intergroup factor. The "Time" variable was taken as the intragroup

factor, divided into three levels: pre-test (T0), three-month follow-up (T3) and five-month follow-up (T5), characterizing the measures of each of the variables in different periods. For hair mineral analysis, as the participants were only evaluated in T0 and T5, *t*-tests for paired samples were performed. In order to verify if there was difference in the means between the groups after the treatment, ANOVA One-Way was performed. For all parameters, $p < 0.05$ was considered statistically significant.

3. Results and Discussion

Baseline characteristics of the groups are presented in Table 1. This sample was divided equally into three groups: G1, G2 and G3. G1 was enrolled as the control group, G2 was to use M-OSA and G3 was to use MMST. No changes to trial outcomes after the trial commenced occurred nor losses of participants or exclusions after randomization. Patients were recruit on April 2017, and follow-up was conducted from May to October 2017, when the period of the study ended.

In order to evaluate the homogeneity of the sample, the three groups were compared at T0. For the dermatological parameters and hair mineral analysis (Tables S1 and S2), in the majority of the evaluated items, the groups did not present at the beginning of the study any statistically significant differences (although it seems to occur in a first look, without statistical analysis). However, in the evaluation of left pore size, users of MMST and M-OSA differed significantly ($p = 0.029$); Significant differences ($p = 0.045$) were also observed for the Truskin® test (left); specifically, the difference was observed between the MMST and M-OSA groups. As groups were not homogeneous at baseline, so this was considered during statistical analysis.

3.1. Transonychial Water-Loss Evaluation

Regarding nail hydration (Table S3), the results indicated significant differences in the time factor; however, in the group factor and in the time x group interaction no significant differences were found. Considering the contrasts, it was observed that there were significant differences between the first application and the following two applications (T3 and T5) both among users of M-OSA and of MMST. However, significant differences were also found between the same times in the control group. Similar results were also observed with respect to hydration of the nails of the hand. In this sense, it appears that the effects are more prone to have occurred due to possible seasonal effects once it started in April (Autumn in Brazil) and ended in September (Spring).

3.2. Skin Multispectral Imaging Evaluation

First, considering the high number of parameters and determinations, non-significative results are expressed in Table S4. For significant results, one can refer to Figure 1. A typical imaging from the multispectral evaluation can be found in Figure 2.
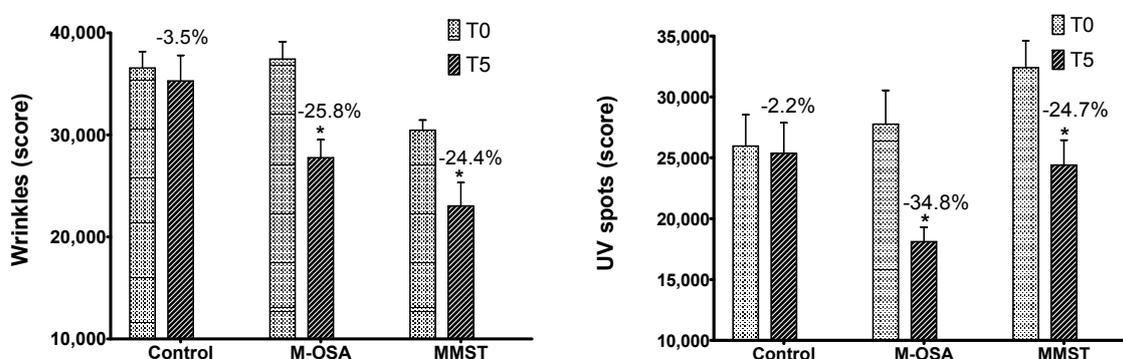

Figure 1. Skin multispectral imaging data for parameters that showed significative results. * Statistically significant difference from T0. G1 = control (placebo). G2 = maltodextrin-stabilized orthosilic acid. G3 = monomethylsilanetriol. T0 = baseline. T5 = 5 months of study.
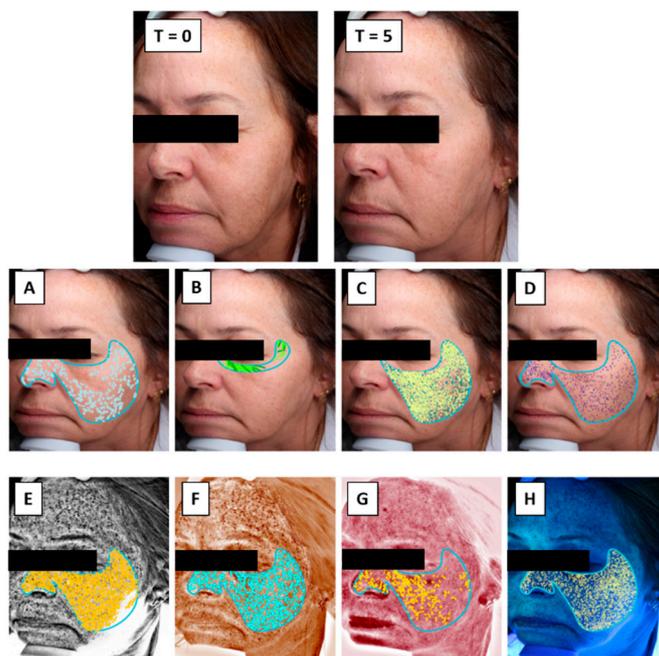
Figure 2. Typical photograph from skin multispectral imaging evaluation. **A** = Spots; **B** = Wrinkles; **C** = Texture; **D** = Pores; **E** = UV spots; **F** = Brown spots; **G** = Red spots; **H** = Porfirines.

Considering the contrasts in the evaluation of wrinkles, it was observed that there were significant differences between the baseline and the two follow-ups, both in G2 and G3, showing that there was a detectable effect on wrinkles betterment. The effect can be attributable to the use of M-OSA and MMST, as no statistically significant differences were found in the participants in the control group.

As what regards UV spots, significant differences were found in the time factor between averages of UV spots (Figure 1). Specifically, the contrasts indicated significant differences on the G2 group between T0 and T5 and between T3 and T5. Among the users in group G3, the results showed significant differences between all the times, i.e., both M-OSA and MMST provided improvement on UV spots and on wrinkles.

For the other factors considered, we have found two situations. For skin texture, size of the pores, length of the eyelashes and cutaneous porphyrins, significative differences were found, but these did occur both for the treatments and for the control—again, this can be related to seasonal effects, once the study was conducted over two seasons. For the other parameters (red areas, brown spots, eyelashes volume and TruSkin Age®), non-significant differences were found in any of the analyses performed (Table S3).

3.3. Hair Mineral Analysis

In the group of participants who used the M-OSA (G2), a statistically significant difference was observed for aluminum (Al), which decreased from 5.34 µg g^{-1} at T0 to 4.96 µg g^{-1} at T5 (Figure 3 for significative results, and Tables S5–S8 for complete results). Silicon (Si) also showed a statistically significant difference, from 80.07 µg g^{-1} at T0 to 85.18 µg g^{-1} at T5. Finally, in relation to the group of participants who MMST (G3), there was a statistically significant difference for aluminum (Al), which decreased from 6.82 µg g^{-1} at T0 to 6.55 µg g^{-1} at T5. Although the statistical tests did not show significant difference in the Si levels in the MMST group, one can verify its increment from baseline to the final timepoint, which is compatible with the effects observed (in both groups).
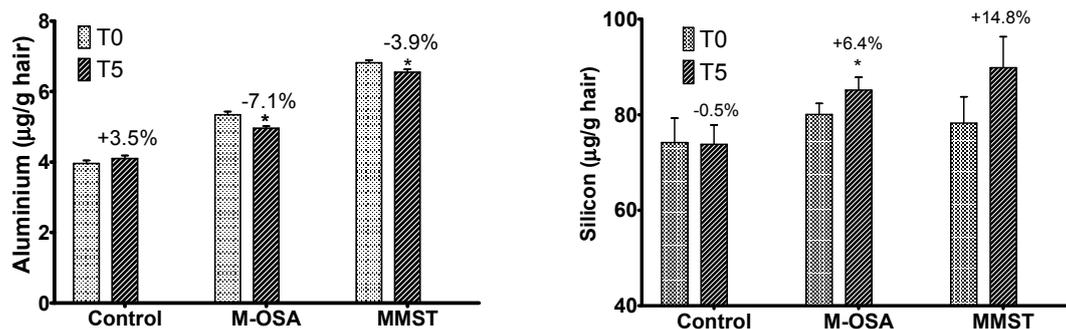
Figure 3. Significative results from hair mineral analysis, as a function of time in the groups. Elements determined as μg per g of hair. * Statistically significant difference from T0. M-OSA = maltodextrin-stabilized ortoshilic acid. MMST = treated with monomethylsilanetriol. T0 = baseline. T5 = 5 months of study.

3.4. Subjective Evaluation

The participants' perception of changes in the skin, hair and nails was assessed through a self-efficacy questionnaire. To evaluate these aspects, the respondents used a scale with values between 1 and 10, in which 1 is considered that there was no improvement and 10 that there was excellent improvement. The results of these analyzes are presented in Table 2. In relation to the control group, only the yellowing of the nails showed a statistically significant difference at T3 and T5. For G2, there was a statistically significant difference for skin oiliness, amount of darkened areas in the skin, speed of whitening of the skin, and nail stains. In relation to G3, a statistically significant difference was observed for the number of darkened areas of the face, wrinkles/lines of expression of the lips, wrinkles/forehead expression lines, hair vitality, and yellowing of the nails. It is worth noting that mean comparison tests were performed for all the variables of the self-efficacy questionnaire, and the results can be seen in the Tables S9–S12.

Table 2. Participants' perception of changes in the skin, hair and nails after treatments (intra-group comparison).

Group	Parameter	T3 (M ± SD)	T5 (M ± SD)	*p*
G1 (*n* = 17)	Nails			
	Yellowing	0.88 ± 1.73	5.13 ± 3.68	0.03
	Skin			
	Oiliness	3.50 ± 3.07	6.00 ± 3.12	0.02
G2 (*n* = 17)	Darkened areas	4.40 ± 2.84	7.30 ± 1.49	0.02
	Whitening velocity	3.90 ± 2.69	6.60 ± 2.63	0.02
	Nails			
	Stains	3.30 ± 3.71	6.20 ± 3.05	0.03
	Skin			
	Darkened areas	3.88 ± 2.42	7.63 ± 2.20	0.04
	Wrinkles/Expression lines (lips)	4.00 ± 2.78	6.11 ± 2.03	0.03
	Wrinkles/Expression lines (forehead)	4.50 ± 3.27	6.90 ± 1.73	0.01
G3 (*n* = 17)	Hair			
	Vitality	6.67 ± 2.61	8.58 ± 1.00	0.03
	Nails			
	Yellowing	3.33 ± 4.56	8.22 ± 2.68	0.05

Scores ranged from 1 to 10 (1—no improvement and 10—excellent improvement). Perception of improvement should be based on the baseline by the volunteers.

M = mean. SD = standard deviation. G1 = control (placebo). G2 = treated with maltodextrin-stabilized ortoshilic acid. G3 = treated with monomethylsilanetriol. T3 = 3 months of study. T5 = 5 months of study.

The difference between the groups regarding the questionnaire of perceived self-efficacy was assessed and the significant results at the end of the study (T5) are presented in Figure 4 (complete results are presented in Tables S9–S12). Bonferroni Post Hoc tests indicated that, for the general appearance of the skin, the participants of the MMST group (G3) differed significantly ($p = 0.02$) from the control group; the same was true for the variable skin hydration ($p = 0.02$). Regarding the homogeneity of the skin, the participants of the M-OSA group (G2) differed significantly from the participants in the control group ($p = 0.05$). Concerning the intensity of the color of the darkened areas the participants of the MMST group (G3) differed significantly from the participants in the control group ($p = 0.01$). For the variable amount of darkened areas, a significant difference was observed among G1 and G2 ($p = 0.002$) and G3 ($p = 0.0002$). For the skin imperfections, the participants in G3 differed significantly from the participants in the control group ($p = 0.04$). The luminosity skin variable, presented a significant difference between the participants of the G3 and the participants in the control group ($p = 0.03$).

Regarding the variables that assessed hair related issues, a significant difference was observed between the participants of G3 and the participants in the control group for the variables: hydration ($p = 0.02$); nutrition ($p = 0.02$); softness ($p = 0.04$); vitality ($p = 0.01$); luminosity ($p = 0.01$); and dandruff ($p = 0.03$). No significant differences were found between the participants in the G2 group and participants in the control group.
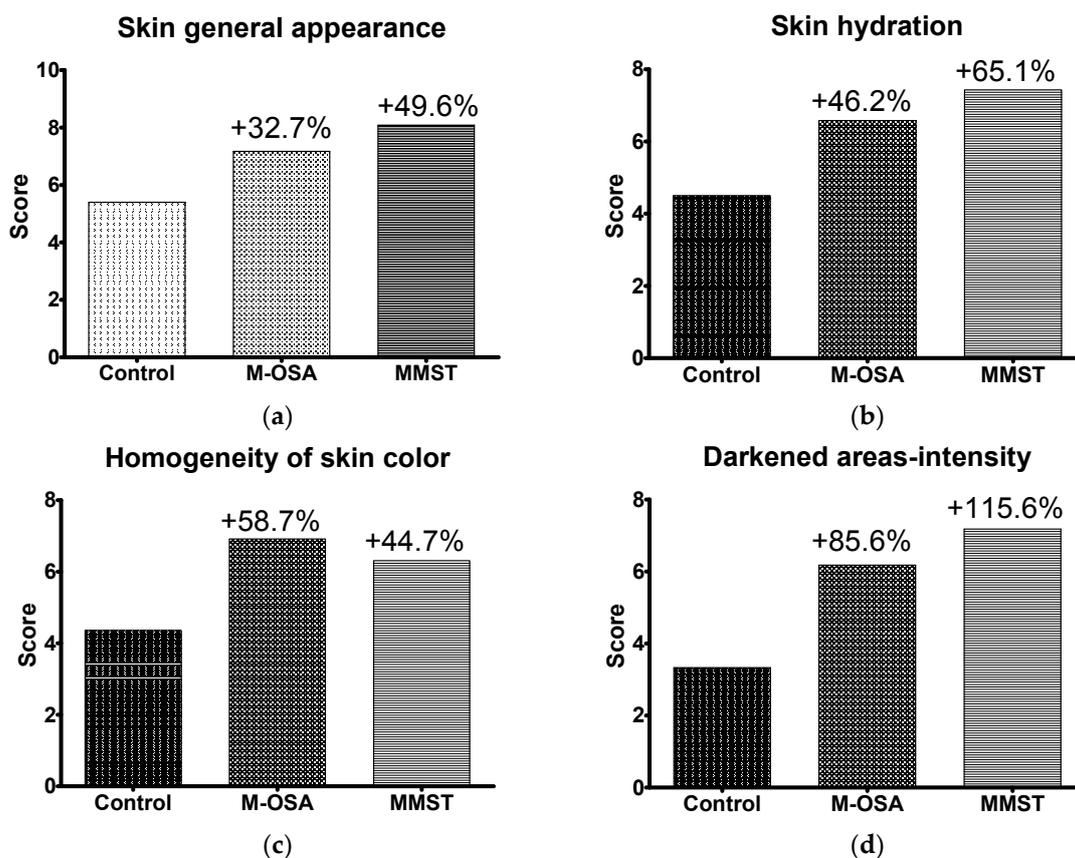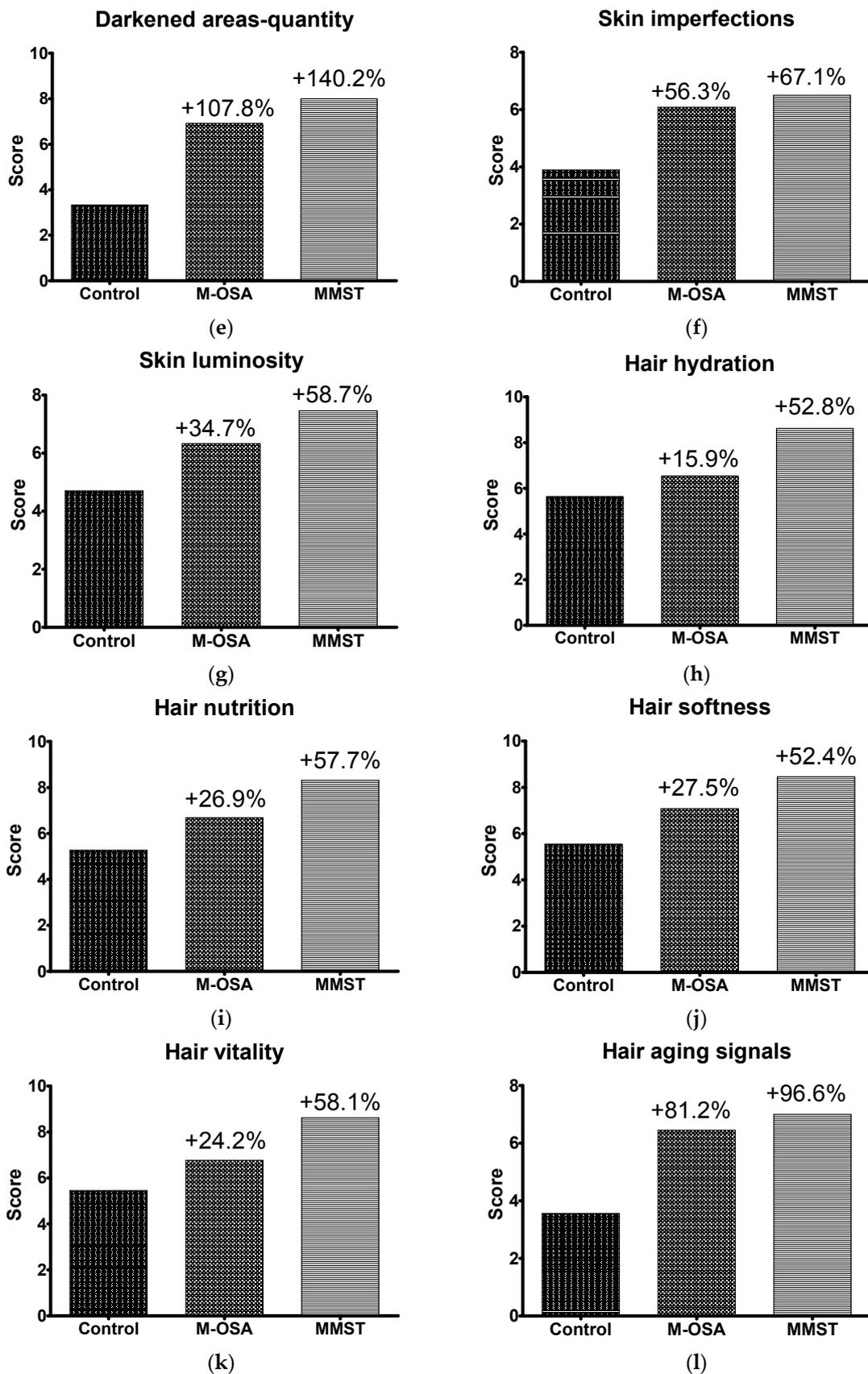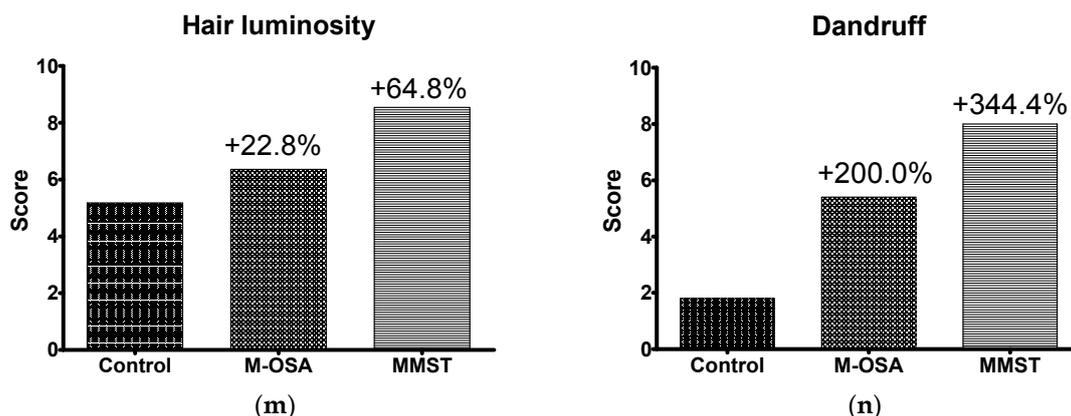

Figure 4. *Cont.*

Darkened areas-quantity

+140.2%

+107.8%

Score

Control   M-OSA   MMST

(**e**)

Skin imperfections

+67.1%

+56.3%

Score

Control   M-OSA   MMST

(**f**)

Skin luminosity

+58.7%

+34.7%

Score

Control   M-OSA   MMST

(**g**)

Hair hydration

+52.8%

+15.9%

Score

Control   M-OSA   MMST

(**h**)

Hair nutrition

+57.7%

+26.9%

Score

Control   M-OSA   MMST

(**i**)

Hair softness

+52.4%

+27.5%

Score

Control   M-OSA   MMST

(**j**)

Hair vitality

+58.1%

+24.2%

Score

Control   M-OSA   MMST

(**k**)

Hair aging signals

+96.6%

+81.2%

Score

Control   M-OSA   MMST

(**l**)

Figure 4. *Cont.*

Figure 4. Comparison of means of self-efficacy questionnaire variables as a function of group at the end of the study (T5). (**a**) skin general appearance; (**b**) skin hydration; (**c**) homogeneity of skin color; (**d**) darkened areas—intensity; (**e**) darkened areas—quantity; (**f**) skin imperfections; (**g**) skin luminosity; (**h**) hair hydration; (**i**) hair nutrition; (**j**) hair softness; (**k**) hair vitality; (**l**) hair aging signals.; (**m**) hair luminosity; (**n**) dandruff. All parameters listed showed significance differences between both treatments and the control.

3.5. Discussion

Silicon as an element (Si) was discovered in 1823 by the Swiss chemist Jacob Berzelius, who isolated it from potassium fluorosilicate (K_2SiF_6) and named it from the Latin *silex* ("quartz"). Although the focus of this work is on its dermatological use, Si is one of the most used elements by humankind, including its use as a semiconductor in electronic components, and as the main component in ceramics, building materials, glass, silicones and other product [19,20]. Its importance in human health has been reported from Louis Pasteur, who was aware of the antiseptic, antimicrobial and antifermentative properties of silicates and predicted that silicon would play a significant role in the treatment of various diseases [21]. However, until a few decades ago the medical emphasis given to Si was directed primarily at the concern about the potential toxicity of its particulate insoluble chemical forms (silicates and crystalline silica), which could cause urolithiasis when ingested orally and especially pneumoconioses (silicosis, asbestosis) caused by inhalation of airborne particles from occupational exposure [19,22,23]. However, more recent experiments and studies employing bioavailable and non-toxic forms of silicon have increasingly contributed to its establishment as a quasi-essential element and/or as a therapeutic adjuvant, emphasizing its structural role in connective tissue and a possible metabolic importance [3,19,24].

Nowadays, silicon-based compounds exist in a high number of commercial products. There is also a current burden of using it for dermatological purposes. Different trademarks and forms to stabilize it are present in the market. In fact, Kalil et al. [18] affirm that one of the diverse Si supplements in the most prescribed oral product for skin rejuvenation in Brazil. However, there is still little evidence on its effects on skin, hair and nails, and the mechanics on the differences found for the many sources of this mineral.

The main point on using Si is its low bioavailability and fixation in the body, reason why there are so many different silicon supplements, each one using a different mechanism to promote better absorption. In general terms, there appear to be two distinct steps involved in biodistribution of dietary silicon after oral absorption: first, the rapid urinary excretion for most of the ingested silicon [9,15,25]; the other step would consist of tissue storage and/or metabolism for the minor part of the ingested Si, proportional to physiological balance [25]. In a human study using Si radioactive, Popplewell et al. [25]. demonstrated that 90% of circulating orthosilicic acid was rapidly excreted without any form of cellular processing. Afterwards, Pruksa et al. [26] reported that ingestion of a dose of soluble dietary silicon by healthy subjects resulted in the same amount being excreted within 24 h. In relation to MMST, it is

kwon that there is a rapid majority urinary excretion, but the storage of minor part of Si occurs for an extended period—and then, there is the bioconversion (metabolism) of MMST to orthosilicic acid (dietary silicon) [17].

To corroborate the importance of the chemical form of silicon, Sripanyakorn et al. [16] studied the comparative absorption of silicon, supplemented as MMST and six other sources which contained high silicon content (non-alcoholic beer, bananas, green beans, orthosilicic acid solution, choline stabilized silicon supplement, colloidal silica and trisilicate of magnesium). The study showed that silicon uptake, based on urinary excretion, was higher for MMST (64% of the dose) and for non-alcoholic beer (60% of the dose), followed by green beans (44%), orthosilicic acid (43%), choline stabilized silicon supplement (17%), bananas and magnesium trisilicate (4%) and colloidal silica (1%). Peak plasma concentration occurred in about 30 min for MMST and green beans, 1.5 h for orthosilicic acid and non-alcoholic beer, 2 h for the choline stabilized silicon supplement and colloidal silica and 4 h for magnesium trisilicate. Monomeric silicates were rapidly absorbed, while particulate silicates presented a decrease in absorption with increased polymerization. The authors concluded that MMST silicon was very well absorbed, presenting higher absorption when compared to the other silicon sources studied.

Similarly, the bioavailability of silicon from M-OSA was previously evaluated by Boqué and Arola [27] and the results showed an approximate oral bioavailability of 30% in terms of elemental silicon. Therefore, the results of this study showed that the absorption of silicon from M-OSA was in percentage terms higher than the values obtained in the study by Spripanyakorn et al. [16] for OSA stabilized on choline, magnesium trisilicate and colloidal silica (respectively 16%, 4% and 1%).

In our study, we used two different forms of Si: M-OSA and MMST. Specifically, we have used the commercial products SiliciuMax® Powder and SiliciuMax® Liquid, respectively, used after quality control tests (assay). M-OSA and MMST did produce an increase in mean hair Si content, but for MMST this did not reach statistical significance. Jugdaohsingh et al. [17] also studied the metabolism of MMST in a 4-week supplementation study, using the blood and urine as biological matrices. Their data showed that 4 weeks of MMST supplementation significantly increased total serum silicon concentrations with median 272 µg/L versus baseline median of 173 µg/L ($p = 0.0002$) or placebo median of 191 µg/L ($p = 0.003$). In urine, total silicon concentrations after silicon supplementation for 4 weeks resulted in an average of 17.0 mg/L versus baseline of 8.5 mg/L ($p = 0.008$) or placebo median of 7.8 mg/L ($p = 0.007$).

We have chosen hair as the biological matrix because of its widespread applications in toxicological, clinical, environmental and forensic investigations [28]. It also reflects long-term exposition, and not the momentary status of a given element within the body, as occurs with the blood. It has a particular interest in the biomonitoring of heavy metals, as it is a vehicle for excretion of such substances because the metal cations are able to bind to the sulphur present in the keratin of the hair matrix [29,30]. In this sense, a related result was found for the use of M-OSA and MMST, as both treatments reduced, after 5 months, the hair levels of aluminum. Magnesium and phosphorus also showed different levels among the three groups, but the effect could not be related to the treatments themselves, only to time. On the contrary, aluminum reduction was actually correlated directly to the consumption of M-OSA and MMST. This effect is in accordance with the literature: epidemiological studies already suggested that silicon can prevent the absorption of aluminum and/or increase its excretion [31–34]. Indeed, in nature, silicon readily forms complexes with aluminum and therefore, aluminosilicates are the most prevalent form of silicates [3]. Reduction of aluminum levels in the body is of sheer importance because of its neurotoxicity, mainly in Alzheimer's disease pathogenesis, and because we live and in a world in which is virtually impossible not to be exposed to such element [35,36]. To the best of the authors' knowledge, this is the first report of the aluminum detox activity for M-OSA and MMST.

Other important result found in our study was the reduction of facial wrinkles and UV spots—the link between sun exposure and hyperpigmentation is clear from the literature, as what occurs in melasma [37]. Recent studies with organic Si stabilized by other chemical forms also shows similar

results. For example, Kalil et al. [18] showed that in a small population, the use of OSA stabilized by hydrolyzed collagen (daily dose = 600 mg) provided positive results on firmness, hydration and skin texture. However, these results were found during the clinical evaluation by the dermatologist, not by multispectral imaging evaluation, although they have used the same device as the one used in this study. No changes in wrinkles or UV spots was found, which corroborated the hypothesis that the chemical form of stabilization the Si really affects its effects on human body.

Barel et al. [6] also evaluated the effects of OSA on skin, nails and hair, but using a molecule stabilized with choline (Si daily dose = 10, during 20 weeks, in 50 women with photodamaged skin). They have assessed the effects of this supplement using a corneometer (to measure skin hydration), a reviscometer (for visco-elastic properties of the skin) and a visiometer (for microrelief/roughness), and also biochemical parameters in serum. They found out an increase in serum Si concentration, and positive effects on skin surface and skin mechanical properties, and on nail fragility, but no mention to wrinkles or UV spots was made.

With concerns to our results, together with the proven effects directly related to Si consumption, skin texture and eyelashes length also changed throughout the study for all groups. These effects can be attributable to the role that Si plays on collagen synthesis (it stimulates type I collagen synthesis), on enzyme activation and cross-linking in connective tissues, and on the increase of elastic fibers density [7,9,21]. The reduction of collagen, proteoglycans and glycosaminoglycans, as well as the degradation of elastic fibers, are key factors on the skin aging, which can be observed as sagging. In addition to that, Si also was shown to provide important connections among hyaluronic acid, proteoglycans and water [38]. All of these data are strong points that corroborates the findings of our study on the betterment of facial skin parameters. What also corroborates the analytical results is the patients' self-reported satisfaction with the treatment, in scale of 1–10. Comparison between control x treatments showed a higher number of parameters well evaluated for the ones who used MMST instead of M-OSA. But in a general manner both treatments were able to provide satisfaction in the volunteers in hair, nail and skin parameters.

To our knowledge, this is the first clinical study on both M-OSA and MMST to evaluate the parameters here described, which adds evidence to what is already in literature for these substances. As future perspectives, one envisions a continuity of this work with a higher follow-up period and a greater sample population, as these were two limitations of the study. Histopathological evaluations are also recommended, as well as the use of enhanced tools to allow the visualization of the results on hair and nail quality.

4. Conclusions

Orthosilicic acid stabilized by maltodextrin (M-OSA) and monomethylsilanetriol (MMST) both provide betterment on facial wrinkles and UV spots and decrease of hair aluminum levels. In addition, overall grades given by the patients to the treatments show that they are suitable products for the market. These data altogether account for positive results regarding dermatology clinical practice for both products.

between the groups for the self-reported questionnaire. Table S10: Comparison of means for chemical variables (self-reported questionnaire), according to groups at zero and five months (T0 and T5, respectively): control group (placebo). Table S11: Comparison of means for chemical variables (self-reported questionnaire), according to groups at zero and five months (T0 and T5, respectively): group treated with maltodextrin-stabilized orthosilic acid (SiliciuMax® capsules). Table S12: Comparison of means for chemical variables (self-reported questionnaire), according to groups at zero and five months (T0 and T5, respectively): group treated with monomethylsilanetriol (SiliciuMax® Liquid).

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