IFSCC 2025 full paper (IFSCC2025-1444)

A biomechanical study of the effects of silicium on the skin

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1. Introduction

In human and animal, silicium is naturally present in connective tissues. Its high affinity for their constituents contributes to their structural conformation [1]. However, with age, silicium intake decreases, and its supplementation is described as beneficial [2].

Bioavailable silicium derivatives, such as orthosilicic acid (OSA) and monomethylsilanetriol (MTS), have gained significant attention for their beneficial effects on connective tissues and extracellular matrices (ECM). These compounds are used across various sectors of health industry: in pharmaceuticals, they serve as components of medical devices that promote bone and skin healing; in nutraceuticals, they support bone mineral density and enhance the health of skin and its appendages; and in dermocosmetics, they are valued for their anti-aging properties on the skin [2-5].

ECMs play a crucial role in maintaining tissue integrity by providing structural support, modulating biomechanical properties such as stiffness and elasticity, and facilitating cell signaling through interactions with integrins. These interactions tightly influence cell behaviors, including survival, proliferation, differentiation, migration [6-8]…

In skin, aging induces dramatic alterations of the ECM, eventually leading to visible clinical manifestations such as wrinkle formation and skin sagging. Among all the documented changes in fibroblasts, the most notable are: a reduction in number, morphological shifts toward a smaller and rounder shape with fewer mechanical contacts to the matrix, an increase in matrix metalloproteinase (MMP) activity leading to a decrease in collagen fiber density, a decline in hyaluronic acid content [8-10]… Taken together, these alterations impair the biomechanical properties of the dermis, particularly its tensile strength and viscoelasticity [8-10].

Atomic force microscopy (AFM) has emerged as a powerful technique for assessing biomechanical properties at both the cell and tissue levels. AFM allows for high-resolution imaging of surface topography and quantification of parameters such as stiffness, viscosity, and adhesion forces, thus providing valuable insights into the structural and mechanical characteristics of biological samples at the nanoscale [11].
We hypothesized that MTS, a silicium-based compound recognized for its matrix-remodeling properties, could restore the mechanical functions of an aged skin by improving the fibroblast–ECM interactions and the collagen architecture. In this study, we therefore assessed MTS ability to restore the skin biomechanical properties using the AFM technology.

2. Materials and Methods

Detection of silicium in human skin: Human skin explants (face lifting from a 69-year-old female Caucasian donor) were cultured at 37°C, 5% CO_2 in Dulbecco's modified Eagle Medium (DMEM) supplemented with 4.5 g/l glucose and antibiotics. MTS was topically applied for 48 h. A 2 mm sample was processed in resin for each condition. The atomic composition of the explant was assessed using secondary ion mass spectrometry (SIMS). The quantitative distribution of silicium 28 (^{28}Si) across different skin compartments reflects MTS distribution.

Cell culture: Normal Human Dermal Fibroblasts (NHDF) were isolated from breast tissue (17 y.o. patient who underwent plastic surgery). Cells were cultured at 37°C and 5% CO_2 in DMEM (4.5 g/l glucose, 10 % Fetal Bovine Serum - FBS) supplemented with Glutamax and antibiotics. All culture media were obtained from Invitrogen and FBS from Biowest.

Treatments of cells: Culture wells were coated with collagen I in the presence of MTS. After 24 h of incubation, wells were washed with phosphate-buffered saline (PBS) and NHDF were seeded in either "optimum" DMEM culture medium (with 10 % FBS) or "suboptimum" DMEM (with 1 % FBS) to mimic aging. After 24 h of incubation at 37°C, cells were fixed in PFA (4%).

2D-*in vitro* study of cell morphology: Following cell membrane permeabilization with PBS/Triton 0.5 %, F-actin was stained using a-rhodamine phalloidin (Invitrogen). Nuclear DNA was counterstained using DAPI (Southern Biotech). Cells were observed with an epifluorescence microscope (Olympus BX60, Japan). For each condition, representative images were taken (20x). Cell shape (size, circularity) was analyzed using the Image J® (version 1.52d) software.

AFM analysis:

Collagen fiber aggregation and anisotropy: The AFM used in this study is a Resolve (Bruker) equipped with a Leica DMi8 (40× objective), enabling correlative studies (AFM/Fluorescence imaging). The Miro/QNM (Quantitative Nanomechanical Mapping) mode was used for this study. The selected AFM cantilever for traction force measurements, mean elastic modulus (Ea), and imaging has a theoretical stiffness constant of 3 N/m in liquid and 6 N/m in air, with a pyramidal tip featuring a 10 nm curvature radius. Before each use, the deflection sensitivity of the probe was calibrated on sapphire, and its stiffness constant was determined using the thermal noise method.

Cell/Matrix interaction forces: The quantitative data of the elastic modulus were extracted from each curve applying Hertz-Sneddon model.

Here, we assumed that our sample was perfectly incompressible so that the Poisson's ratio used was 0.5. However, since neither the Poisson's ratio nor the tip shape were accurately known, we report in this work only an 'apparent modulus' (Ea). The experimental conditions being the same for all studied samples, Ea could be used for comparisons at a high degree of confidence. The quantification of the elastic modulus from raw force curves was performed using BioMeca Analysis software.

$$F = \frac{2}{\pi} \cdot \frac{E}{1-\nu^2} \cdot \tan(\alpha) \cdot \delta^2$$

F is the force from force curve, **E** is the Young's modulus, **v** is the Poisson's ratio, α is the half angle of the indenter and **δ** is the indentation.

Test on human skin explants: Human mammary skin explants were obtained from Biopredic, Rennes (France). Young and aged skins come from a 31 and a 51 y.o. Caucasian woman respectively. Explants were maintained in a DMEM supplemented with glucose 4.5 g/l and antibiotics, and received a daily topical treatment with MTS for 48 h.

Detection of collagen I: Formalin-fixed 5 µm sections were incubated with a polyclonal anti-human collagen I antibody (Southern Biotech), and with a fluorescein isothiocyanate (FITC)-labelled secondary antibody. Nuclei were stained with an Ultracruz mounting medium with DAPI. Sections were observed with an epifluorescence microscope (Olympus BX60, Japan). For each condition, representative fields were selected from 3 punch biopsies, and 3 images were taken (10x). Computer-assisted image analysis was achieved with the Cell F software (Olympus, Japan).

High-resolution imaging of the papillary dermis: Topography imaging highlights the organization of structures such as the collagen network. For this purpose, the study was

conducted using AFM in air using a conical tip with a stiffness constant of 0.4 N/m. Scans over a few microns were performed to visualize the organization of collagen fibers on cryosections.

Viscoelasticity analysis by AFM: Human skin explants were obtained from abdominal skin of 55 and 60 y.o. Caucasian females who underwent plastic surgery. Skin punches of 120 mm in diameter were cultured at 37°C, 5% CO_2 in DMEM supplemented with antibiotics. MTS was topically applied (40 µl per punch, twice daily) for 48 h. AFM measures were done on 30 min stabilized room humidity explants AFM measurements were performed on explants equilibrated for 30 minutes at room humidity.

Clinical study: 37 volunteering women aged 32 to 60 (mean age: 49 y.o.), who presented wrinkles or fine lines received a daily treatment with a cream containing 0.015% MTS on the face for 28 days. At day 0, 14 and 28, a dermatologist assessed skin hydration, firmness, elasticity, aging signs, texture of cutaneous relief, and the skin tone using a standardized scoring method.

3. Results

MTS penetrates the skin and reaches the dermis

In order to assess the ability of MTS to penetrate the skin and reach the ECM, MTS was topically applied to human skin explants for 48 h. The amount of silicium in the different skin compartments was then quantified using SIMS.

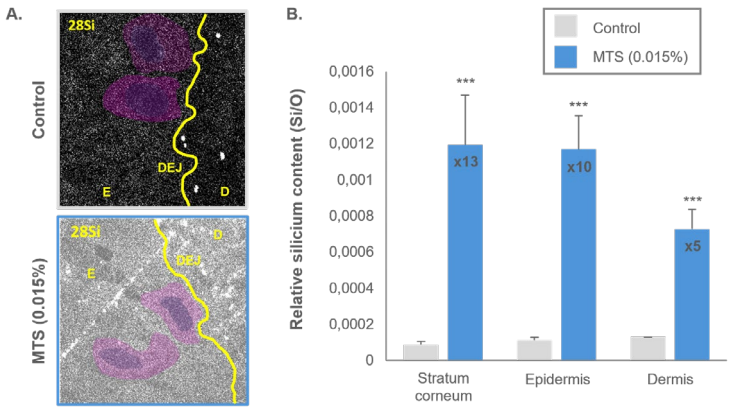

Figure 1 – Topically applied silicium penetrates the skin. SIMS pictures of human skin explants treated with MTS (0.015%). The silicium (^{28}Si) was observed (A) and quantified in each skin compartment (B). ***p-value<0.001. Cell cytoplasms are highlighted in pink and cell nuclei in purple. E: Epidermis, D: dermis, DEJ: yellow line.

Treatment with MTS dramatically increased the silicium detection across all skin layers analyzed. Quantitative analysis revealed, in comparison to the control condition, a 13-fold increase in the stratum corneum, a 10-fold increase in the viable epidermis, and a 5-fold increase in the dermis compared to untreated controls (Figure 1).

MTS preserves youthful fibroblast phenotype

Serum deprivation, used here as a model for fibroblast aging, led to marked alterations in cell morphology compared to control fibroblasts cultured in the presence of serum. Aged fibroblasts exhibited a significant reduction in cell size (Figure 2A, B) and showed impaired spreading with a more rounded appearance (Figure 2C).

Pretreatment with MTS for 24 h on collagen I-coated substrates effectively counteracted these morphological alterations. Fibroblasts pretreated with MTS retained a morphology comparable to control (young) cells, maintaining both cell size and a more elongated shape. Notably, MTS significantly reduced the circularity index induced by serum deprivation, suggesting preservation of cytoskeletal integrity and cell-ECM interactions (Figure 2).

These findings indicate that MTS exerts a protective effect on fibroblast morphology under stress conditions mimicking aging.

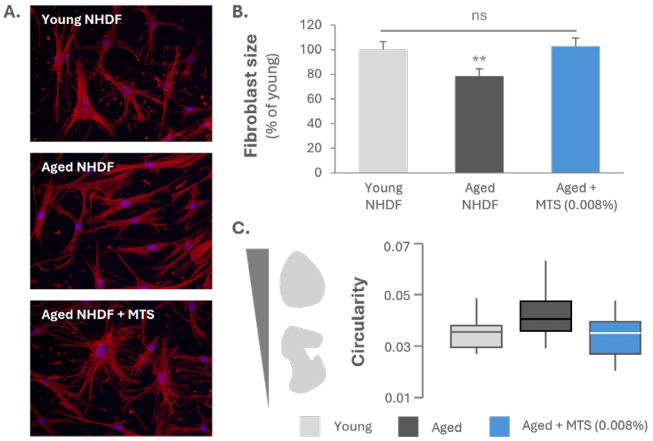

Figure 2 – MTS preserves fibroblast morphology. Young or aged NHDF were plated on collagen-coated wells in the presence or in the absence of MTS. Fibroblast shape was observed (A, actin appears in red (rhodamine-phalloidin) and cell nuclei in blue (DAPI)), and their size (B) and circularity (C) measured. ns: non-significant, **p-value<0.01 vs young NHDF, n=30.

MTS improves cell–matrix interactions

In addition to morphological alterations, aging also impairs fibroblast mechanical function, particularly their ability to interact effectively with ECM fibers.

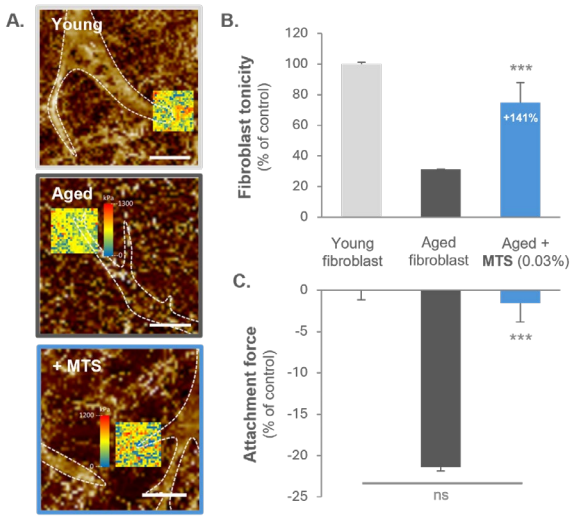

Figure 3 - MTS restores fibroblast ability to bind collagen fibers. Microphotographs of NHDF plated on collagen fibers pretreated with MTS for 24h (A). Fibroblast tonicity (B) and attachment force (C) were measured using AFM. *** p-value<0.001 vs. Aged NHDF, n=10.

This weakening of fibroblasts contributes to compromised tissue architecture and reduced mechanical integrity [12]. Quantitative AFM analysis revealed that aged fibroblasts exhibit a 69% reduction in mechanical strength compared to young fibroblasts, resulting in an approximately 20% decrease in attachment force between cells and collagen fibers (Figure 3A–C).

Remarkably, pretreatment of the collagen I coating with MTS significantly preserved fibroblast adhesion capacity. Cells seeded onto MTS-coated matrices maintained stronger cell-fiber interactions despite serum deprivation, with adhesion forces approaching those observed under control conditions. These results suggest that MTS enhances or stabilizes integrin-ECM engagement.

MTS prevents aged-related collagen fiber aggregation and restores fiber anisotropy

Aging in the ECM is associated with fiber aggregation driven by non-physiological cross-linking processes [13,14], leading to tissue stiffening and disorganization. In our model, aged fibroblasts induced significant collagen fiber thickening compared to young fibroblasts (Figure 4A,B).

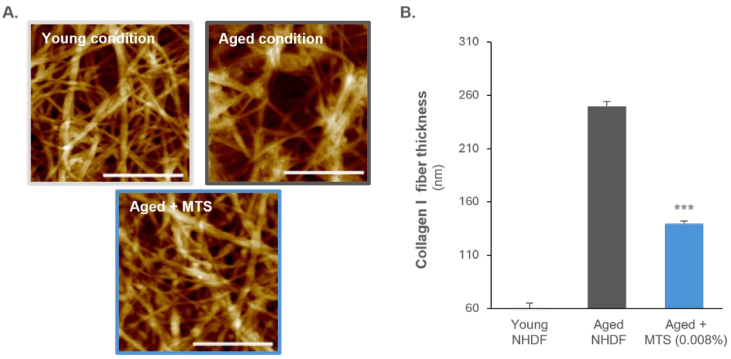

Figure 4 – MTS prevents collagen fibers aggregation.
Collagen fibers were pretreated with MTS for 24 h. NHDF were then plated for 24 h. The fibers were observed (A) and their thickness was measured (B) using AFM. *** p-value<0.001 vs. Aged NHDF, n=10.

Pretreatment of collagen-coated substrates with MTS significantly limited this age-related fiber aggregation. MTS reduced collagen thickening by 58% compared to the aged control, partially restoring fiber morphology toward a youthful profile (Figure 4B), suggesting that MTS helps preserve matrix architecture.

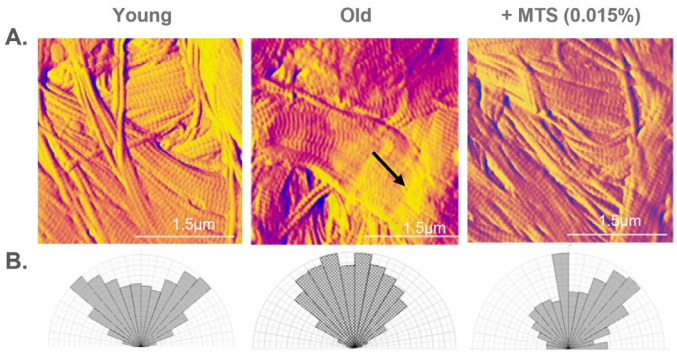

Figure 5 – MTS improves the fibers anisotropy.
Fibers from the papillary dermis from a young or an aged donor that received a treatment with MTS were observed (A) and the anisotropy was assessed (B) using AFM.

Ex vivo study confirmed a loss of collagen fiber anisotropy in the papillary dermis of aged donors, with less organized and more aggregated fibers compared to younger skin (Figure 5). A 48 h topical application of MTS (0.015%) restored anisotropy, producing sharper, multidirectionally oriented fibers resembling those in young tissue.

Overall, these findings demonstrate the ability of MTS to mitigate age-induced ECM disorganization by reducing collagen aggregation and restoring fiber alignment.

MTS increases collagen I deposition in the papillary dermis

Silicium has been shown to stimulate collagen I synthesis in fibroblasts and osteoblasts [15]. To evaluate the effect of MTS on dermal collagen deposition, an *ex vivo* model using skin explants from an aged donor (51 years old) was used.

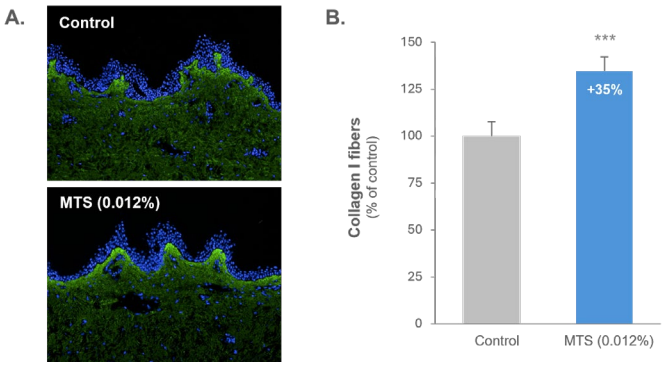

Figure 6 – MTS improves collagen production. Microphotographs of human skin explants treated with MTS (0.012%) for 48 h. The amount of collagen I (in green) was observed – nuclei appear in blue (A) and quantified (B). Mean±SEM. ***p-value<0.001 vs. control.

Topical application of MTS (0.012%) for 48 h led to a 35% increase in collagen I content within the dermis, with a pronounced effect observed in the papillary dermis (Figure 6A,B). This result suggests that MTS may contribute to the restoration of ECM density in aged skin.

MTS improves the viscoelasticity of aged skin

Both collagen content and fiber organization play key roles in maintaining the viscoelastic properties of the dermis. In *ex vivo* skin samples, a marked reduction in viscoelasticity was observed in the papillary dermis of an aged donor compared to that of a younger individual (Figure 7).

Topical treatment with MTS (0.015%) for 48 hours led to a partial yet significant restoration of dermal viscoelasticity. This improvement suggests that MTS also contributes to the functional recovery of the skin's mechanical properties.

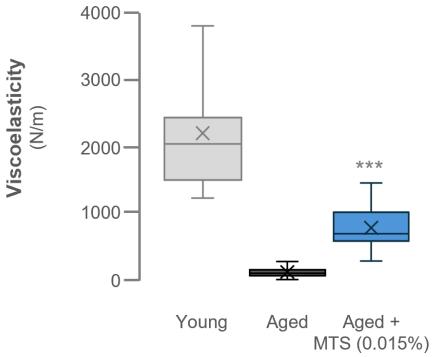

Figure 7 - MTS restores the dermis viscoelasticity. Evolution of the papillary dermis viscoelasticity of human skin explants treated with MTS (0.015%). "X" : mean ; "-" : median ; ***p-value < 0.001 vs aged. n=3.

MTS improves firmness, elasticity, and hydration in a clinical study

The *ex vivo* results were further confirmed by a clinical study performed on volunteers aged 40 to 59 who received a daily treatment with a cream containing MTS for 28 days.

Clinical assessments demonstrated significant improvements in key skin parameters, including firmness, elasticity, and hydration (Table 1), thus confirming the potential of MTS to improve both the structural and functional quality of aging skin.

	Skin parameter	D14		D28	
		Subjects with improvement	Average improvement	Subjects with improvement	Average improvement
Anti-aging	Hydration	97.3%	+13.8% **	100%	+24.1% ***
	Firmness	81.1%	+4.0%	95.6%	+3.8%
	Elasticity	62.2%	+4.0%	86.5%	+3.8%
	Texture	94.6%	+12.0% **	100%	+20.0% ***
	Wrinkles	62.2%	+7.7%	64.9%	+12.0%
Skin tone	Luminosity	100%	+14.8% *	100%	+25.9% **
	Radiance	83.8%	+14.8%	100%	+22.2% **
General appearance / Signs of aging		97.3%	+11.5% *	100%	+23.1% ***

Table 1 – MTS provides global benefits. Clinical evaluation of several skin parameters. *p-value<0.05, **p-value<0.01, ***p-value<0.001 vs D0.

4. Discussion

The findings of this study demonstrate that MTS, a bioavailable form of silicium, exerts restorative effects on the structural and biomechanical properties of aged skin. These observations are consistent with prior reports that bioactive silicon supports ECM homeostasis in connective tissues, including the dermis [3,4].

Aging skin is characterized by profound changes in the ECM, as decreased fibroblast activity, reduced collagen synthesis, fragmentation of fibers, and increased non-enzymatic crosslinking. These alterations collectively compromise the biomechanical properties of the dermis such as elasticity and mechanical resilience [8,9].

SIMS analysis revealed clear evidence of silicium penetration following a topical application of MTS on the skin. This spatial distribution supports the hypothesis that MTS is delivered across the skin barrier and reaches biologically relevant layers as described in the literature [16]. The ability of MTS to reach the dermal compartment is particularly noteworthy, as it is home to fibroblasts, the cells responsible for collagen production and skin matrix remodeling—key targets in anti-aging skincare strategies.

In vitro, MTS preserved fibroblast morphology under serum deprivation—a model of cellular aging—by maintaining cell size and reducing circularity. This suggests that MTS supports fibroblast-ECM interactions and may counteract age-related cellular senescence [12].

Using AFM, we further showed that aged fibroblasts promote abnormal collagen aggregation and fiber thickening, mimicking age-associated ECM disorganization. Remarkably, MTS limited this aggregation and restored collagen fiber anisotropy in *ex vivo* models—an important parameter of ECM organization, suggesting that it may help stabilizing collagen architecture and promote a better organized ECM. It may therefore contribute to improving mechanical strength and tissue resilience [11].

On top of improving ECM organization, MTS also enhanced collagen I deposition, especially in the papillary dermis, which further confirms its capacity to stimulate matrix renewal [15,17]. This dual effect may help explain the improvements observed in collagen fiber alignment and dermal flexibility, which were restored by MTS treatment. This observation is consistent with previous data on silicium's role in modulating collagen synthesis and organization [15,17].

Moreover, a potential mechanism through which MTS may exert its effects involves the reactivation of certain cellular adhesion pathways, particularly those involving integrins—most notably β1-integrin—and the focal adhesion kinase (FAK) signaling pathway. These systems are essential for maintaining fibroblast organization and their connection to the surrounding ECM [18]. By preserving these cellular adhesion mechanisms—especially focal adhesion sites and actin network organization—MTS could help fibroblasts continue to sense and respond to mechanical cues, which is crucial for efficient ECM remodeling and maintaining collagen fiber alignment. While this remains a working hypothesis, it provides a possible explanation for the observed improvements in ECM dynamics and skin biomechanical properties.

AFM-based measurements of dermal viscoelasticity confirmed that MTS improves not only ECM structure but also its biomechanical performance. Given that viscoelasticity decreases significantly with age, these findings are particularly relevant for maintaining skin's ability to resist deformation and mechanical stress [9].

The clinical study confirmed the translational relevance of these results. Daily application of a formulation containing MTS (0.015%) over 28 days led to measurable improvements in skin firmness, elasticity, and hydration, along with visible reductions in wrinkles and enhanced facial contour.

Taken together, these data highlight the added value of atomic force microscopy as a precise and sensitive tool to quantify biomechanical markers of skin aging for assessing the efficacy of dermocosmetic active ingredients and position MTS as a promising cosmetic active capable of mitigating age-related ECM degradation and restoring the biomechanical and structural integrity of the skin.

5. Conclusion

This study demonstrates that MTS, a bioavailable silicium derivative, improves fibroblast function and promotes collagen synthesis and organization, thus contributing to maintaining optimal skin biomechanical properties. By targeting both the structural components of the dermis and the functional performance of the ECM, MTS is confirmed as a valuable active ingredient for cosmetic formulations aimed at preventing or reversing visible signs of skin aging.

6. References

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