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ORIGINAL CONTRIBUTION

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Influence of hyper-harmonized fullerene water complex on collagen quality and skin function

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Abstract

Background: Fullerene water complex establishes the optimal order and function of biomolecules in natural, biophysical way by transducing the signal through water hydrogen bonds to biomolecules.

Objectives: This paper considers the effects of the patented hyper-harmonized-hydroxylated fullerene water complex (3HFWC) on biophysical properties of the skin collagen molecules.

Method: Optomagnetic imaging spectroscopy (OMIS) has been used for the analysis of the biophysical skin properties (diamagnetic/paramagnetic) after applying three groups of different cosmetic products. Tested cosmetic products were prepared by replacing the active ingredients with 3HFWC or with water in four commercial products. The original commercial creams and their vehiculums with water added served as control groups. Data were statistically analyzed using paired *t* test in R software.

Results: *t* Test gave statistically significant results for all of the products with 3HFWC, while within the control group, only body lotion and hand cream did show statistically significant results ($P < 0.05$). Significant improvements in abundance and quality of collagen in the dermis were achieved with body lotion with 3HFWC (p^+/p^- ranged from 0.82 to 0.97). While body lotion vehiculum made collagen-water interaction more stable (p^+/p^- ranged from 0.3 to 0.55), hand cream with 3HFWC made it more dynamic (p^+/p^- ranged from 0.63 to 0.49). Body lotion vehiculum improved the compactness of the dermis (p^+/p^- ranged from 0.2 to 1.03), as well as commercial hand cream (p^+/p^- ranged from 0.28 to 0.85).

Conclusion: Compared to the control groups, cosmetic products with 3HFWC demonstrated positive effects on the biophysical properties of the skin. Increased paramagnetic properties are linked to more unpaired electrons, their faster movement, and, finally, better signal transduction. Thus, products with 3HFWC could enable faster regeneration of collagen and prompt skin reaction to the negative environmental influences.

KEYWORDS

collagen, functionalized fullerenes, OMIS, skin care

1 | INTRODUCTION

Fullerene-C_{60} is a type of carbon nanomaterial with spherical cage structure consisted of 60 carbon atoms according to icosahedral symmetry group. It is the third allotropic modification of carbon (like diamond and graphite) found in nature.[1] Unique properties of C_{60} make this molecule widely applicable in different fields of medicine. Due to its insolubility in water and polar solvents, as well as toxic and genotoxic potential (because double bonds may open under certain condition), in last decades various types of functionalized fullerenes have been created and tested for different applications.[2,3] They are currently being studied for the purposes of drug delivery, targeted imaging in diagnostics, free radicals scavenging, and as antioxidant active ingredients.[4,5] Functionalized fullerenes are also being used in cosmetic products for antiaging, whitening, and cellulite control, in moisturizing face creams, sunscreens, etc.[6-8]

Fullerene water complex (3HFWC) or nano-harmonized substance (NHS) is a patented material made by the functionalization of C_{60} molecule with OH groups (C_{60}(OH)x) and through the addition of OH groups by water layers (wNHS) $C_{60}(OH)_{36 \pm 12}@(H_2O)_{144\text{-}2528}$ (Figure 1).[9] These water layers—water liquid phase $(H_2O)_{144\text{-}2528}$, surrounding the solid phase—hydrogen bonded $C_{60}(OH)_{36 \pm 12}$ nanostructure, possess similar properties to the liquid crystalline.[10] They protect $C_{60}(OH)_{36 \pm 12}$ complex from the environmental influences, and at the same time, they protect biomolecules from the potential toxic effects of the C_{60}. This structure, whose diameter size ranges between 8-12 nm, is water soluble amphiphilic biomolecule with a potential for various applications.[11] Fullerene derivative nano-harmonized $C_{60}(OH)_{36 \pm 12}$ has shown no toxicity in tests on human dermal fibroblasts (HDF) and liver carcinoma (HepG2) cells.[1,12] As a cosmetic product ingredient (INCI name is "hydroxylated fullerene"), it could act as an active compound and a stability factor in the commercial cosmetic products.

Fullerene-C_{60} and its derivatives (hydroxylated fullerenes—fullerols) have classical and quantum properties. Fullerene-C_{60} is the largest classical object with quantum effects in the nature.[13] Thanks to their dual properties, fullerenes influence the skin on nano-quantum level, in the classical way—through energy transfer, and in the quantum way—through wave function (energetically-informationally). This molecule rotates in solution 18 billion times per second, while in solid state it rotates 30 billion times per second and it has 46 vibration modes. While quantum properties dominate in atoms, molecules and tissues in human body (~90%, 80% and 60% respectively), classical properties dominate on the organ level (skin) and the whole body (~60% and 90% respectively). In order to investigate the effects of fullerenes, such as 3HFWC, on the skin, skin structure needs to be observed from a different perspective. Quantum properties and changes on the molecule and tissue level thus have to be examined with a proper method that enables measurements of these effects.

Collagen is the most abundant protein in human body.[14] It is present in the extracellular matrix of the skin dermis and makes 75% of total weight. When two amino acids react to form peptide, they make peptide plane, which becomes a biophysical object with quantum properties.[15] On the nano level, collagen fibers possess both quantum and classical features. Collagen is very important as a supportive structure of the skin. The border line between epidermis and dermis, basement membrane, is made partly of collagen fibers. Two types of collagen, collagen type I and type III, are located under the basement membrane, in the dermis, lying parallel to the basement membrane, and collagen types IV and VII are underlying/anchoring those collagens directly to the basement membrane (Figure 2). Peptide plains of these types of collagen molecules are perpendicular and oscillate under the Fibonacci law in young skin with normal-structured molecules.[16] The oscillatory modes of the peptide plains have to be harmonized in order to preserve quality and the function of the skin.

Many factors, such as UV rays, blue light, pollution, and aging, can harm or destroy collagen fibers. Skin becomes untight, loses tonus, and gets wrinkles. When basement membrane, due to the aging process, becomes flat, and many cells in basal layer of the epidermis lose proper nutrient and oxygen supplies, skin needs more time to regenerate. Unpleasant esthetic appeal, cellulite is a consequence,

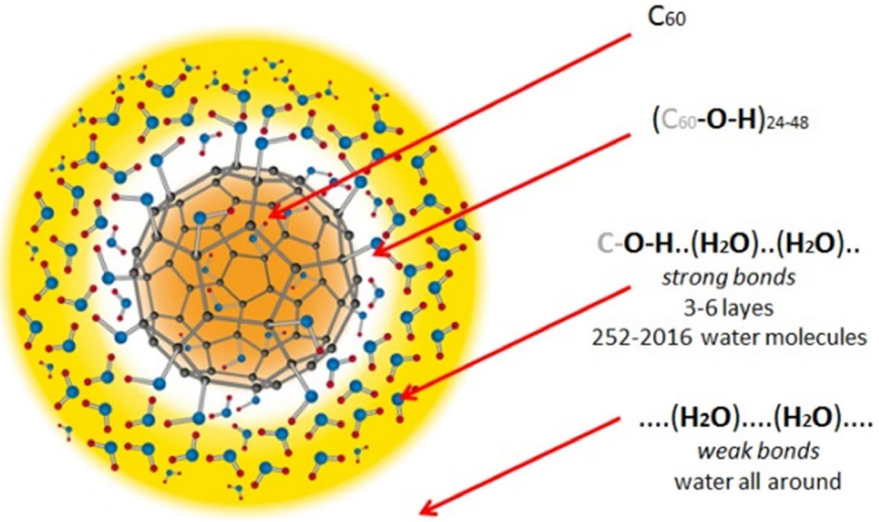

FIGURE 1 The structure of 3HFWC: 3H—hyper-harmonized-hydroxylated and polarized, F—fullerene core C_{60}, W—water, C—complex stabilized with hydrogen bonds under the influence of oscillating magnetic field according to the Fibonacci law (Φ/ϕ):$[C_{60}(OH)_x@(H2O)_y]^{\Phi/\phi}$

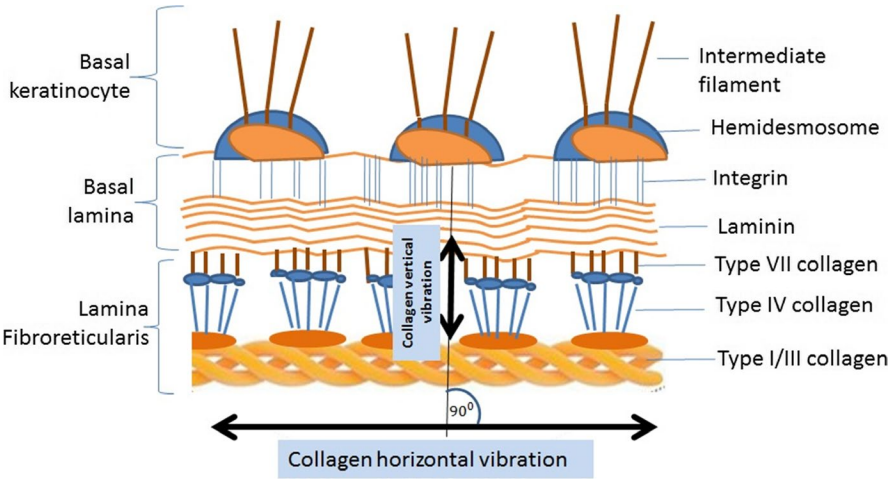

FIGURE 2 Schematic image of the basement membrane. Collagen type I and type III in the dermis (vibrate horizontally) and collagen type IV and VII (vibrate vertically), oscillate perpendicular, under the Fibonacci law in young skin

partly, of altered structure and function of collagen molecules in hypodermis of the skin. It is possible to improve these conditions through various products/methods. 3HFWC, as a structure with the natural icosahedral symmetry, acts biophysically by harmonizing the oscillatory processes of peptide plains in collagen fibers and improves quality and appearance of the skin directly or through water molecules and hydrogen bonds.[1,9,16] According to the previous investigations, hydrogen bonds of water around the dysfunctional biomolecule could force it to oscillate in its natural state.[1] Fullerene water complex applied to the skin through cosmetic product imparts the Golden Mean driving force of a natural self-assembly process (oscillation by icosahedral symmetry law) and establishes the optimal order and function of biomolecules thanks to water molecules.[16,17] At the same time, this structure encourages the function of fibroblast cells in the dermis and increases the collagen and other fiber production.[18] It is important to emphasize that this is enabled through natural physical and not chemical mechanism of information and energy transfer through water hydrogen bonds, in which case the transfer of information and energy to the certain distance without direct physical contact between fullerol and biomolecule is possible. Although it cannot pass through the basement membrane, 3HFWC can improve the quality and quantity of collagen molecules in the dermis.[19,20]

In this study, potentially positive effects of the fullerene water complex on collagen molecules and biophysical properties of the skin have been investigated. Based on the results reported in previously conducted studies, cosmetic products with 3HFWC are expected to improve the quality and quantity of collagen and other fiber molecules, repair function of the basement membrane, and finally, increase firmness and elasticity of the skin compared to the commercial products without fullerene water complex and vehiculum with water.

2 | MATERIALS

Three groups of cosmetic products were used and analyzed in this study. Cream base for all three groups of investigated products was O/W (oil in water) type emulsions. First group of cosmetic products named "vehiculum" presents corresponding vehiculum mixed with the proper amount of water (Table 1) and is referred to as placebo group. Second group integrated commercial cosmetic products named regenerating cream, anti-ageing cream, body lotion, and hand cream (Intercosmetica, Switzerland). These two groups of products were compared with the cosmetic products (testers) made of cream base in which fullerene water complex (3HFWC, TFT Nano Center, Serbia) was added in percentages shown in Table 1. In the same percentages, active cosmetic ingredients with emollient/humectant/conditioning effects on the skin (based on the purposes of the product), together with preservatives and perfume composition, are contained in commercial products.

The study was conducted on 38 volunteers with no dermatologic diseases. Subjects' age ranged from 31 to 69 years (mean age of the participants was 41.3). All enrolled subjects have signed written consent for participation in the study. Subjects were randomly assigned into one of the following three groups:

1. Group I was made of 28 subjects who used cosmetic products with 3HFWC.
2. Group II was made of 5 subjects who used commercial cosmetic products.
3. Group III was made of 5 subjects who used the cream made of vehiculum and water (placebo group).

TABLE 1 Cosmetic products used in this study

Vehiculum—cream base	Commercial products	Products with 3HFWC
vehiculum + 9% water	Regenerating cream	vehiculum + 9% 3HFWC
vehiculum + 10% water	Anti-ageing cream	vehiculum + 10% 3HFWC
vehiculum + 12% water	Body lotion	vehiculum + 12% 3HFWC
vehiculum + 8% water	Hand cream	vehiculum + 8% 3HFWC

Cosmetic products were always applied to the same place, to the inner side of the left forearm and to the outer side of the left hand. Regenerating cream, anti-ageing Cream, and body lotion were applied to the left hand positions marked 1, 2, and 3, respectively, on the Figure 3, while hand cream was applied to the outer side of the left hand. Right hand has not been treated with any product and served as control area. Products were applied every day at the same time during four weeks.

Measurements of biophysical skin properties (diamagnetic/paramagnetic) were done by OMIS before any product was applied, that is at the beginning of the study, and were repeated every 7 days in the following four weeks. Measurements were done under controlled conditions: temperature 22 1°C; humidity 30 ± 2%, average value of environmental electric and magnetic fields: 5,82 V/m and 28,10 nT, respectively.

3 | METHODS

In order to examine the effect of nanocosmetic products on the skin, optomagnetic imaging spectroscopy (OMIS) was used. Optomagnetic imaging spectroscopy is a method for characterization of different types of material, based on light-matter interaction.[21] Optomagnetic imaging spectroscopy device consists of a customized housing with integrated camera and light emitting diodes. Since different wavelengths can penetrate to the different depths of the skin (blue light—stratum corneum, green light—stratums granulosum, spinosum, and basale, and red light—dermis), two types of light emitted by light diodes were used to explore different layers of the skin in terms of its biophysical state: UV and white diffuse light (Figure 4). OMIS method detects paramagnetic/diamagnetic properties of the matter (paired and unpaired electrons in tissue) by convoluting spectra in the R, G, and B channels in the digital image of the skin when the skin is exposed to white diffuse light and white polarized light, as well as white diffuse light and UV light combined.

By subtracting histograms of red (R) and blue (B) color channels in the image of the skin illuminated with white diffuse light (W) and image of the skin illuminated with white diffuse light under Brewster's angle when polarization occurs (P), dermis and epidermis with basement membrane and without stratum corneum can be reached ((W-P) (R-B) spectra). While dermis state is captured within the (W-P)(R-G) spectra, in order to show collagen-water interaction, the combination of white diffuse light and UV light is employed, through the convolution (UV-w). In this investigation, the focus was on collagen in the basement membrane and the dermis.

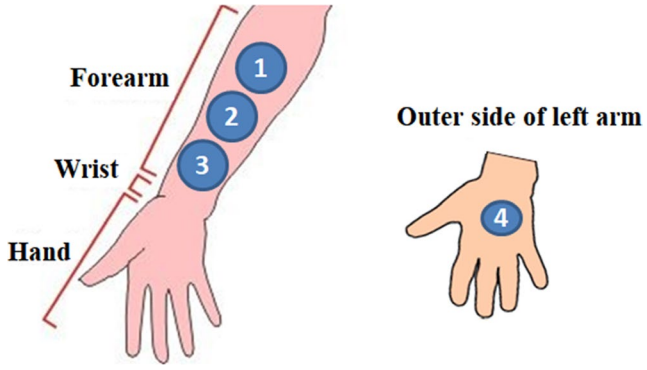

FIGURE 3 Application sites: the inner side of left forearm and the back of the left hand

The effect of each cosmetic product was measured through the ratio values of the area below the positive p^+ (paramagnetic—unpaired electrons) and negative area p^- (diamagnetic—paired electrons) in optomagnetic spectra of the sample (p^+/p^-) obtained by OMIS.

Decrease of p^+/p^- values in (W-P)(R-B) and (W-P)(R-G) spectra indicates increase in diamagnetic properties, better stability, and higher density of the skin structure, while in the case of (UV-w) spectra, increase of ratio value of p^+/p^- indicates higher number of unpaired electrons, their better mobility and faster information transfer through the skin structures. When paramagnetic properties dominate, skin reacts faster to various internal and external influences and its protective potential is improved.

Paired *t* test was used for the before and after observation comparison. *P*-values < 0.05 were considered statistically significant. Data were statistically analyzed in R software environment for statistical computing and graphics.

4 | RESULTS

Optomagnetic spectra of the skin treated with cosmetic products were obtained by optomagnetic imaging spectroscopy. Based on the parameters in the optomagnetic spectra, the analysis of the effect of different products on skin was conducted. Statistical analysis using paired t test gave significant results for the data shown in Table 2. Because of the small number of participants in the study, particularly in control groups, the results were analyzed with caution and used as a guideline for further research. Not all of the tested cosmetic products demonstrated statistically significant improvement, and therefore, only the significant results are discussed in the following sections.

The effect of the *regenerating cream with 3HFWC* on the skin has been analyzed by the utilization of white diffuse light and polarized white light. The p^+/p^- ratio in the dermis spectrum (W-P)(R-G) became more compact after the treatment (less unpaired electrons), while the skin in general (epidermis and dermis, with basement membrane depicted in the (W-P)(R-B) spectra) became more electronically mobile, with the increased movement of unpaired electrons. It means that *regenerating cream with 3HFWC* substance primarily acts on epidermal level and basement membrane.

Results obtained for *anti-ageing cream with 3HFWC* analyzed with UV light indicate that collagen-water interaction becomes more stable after the skin is treated with this product (dynamics of p^+/p^- is 0.51 after the treatment, representing its equilibrium, while before the treatment it was 0.74). This means that the communication between skin structures is improved. Also, skin becomes stable

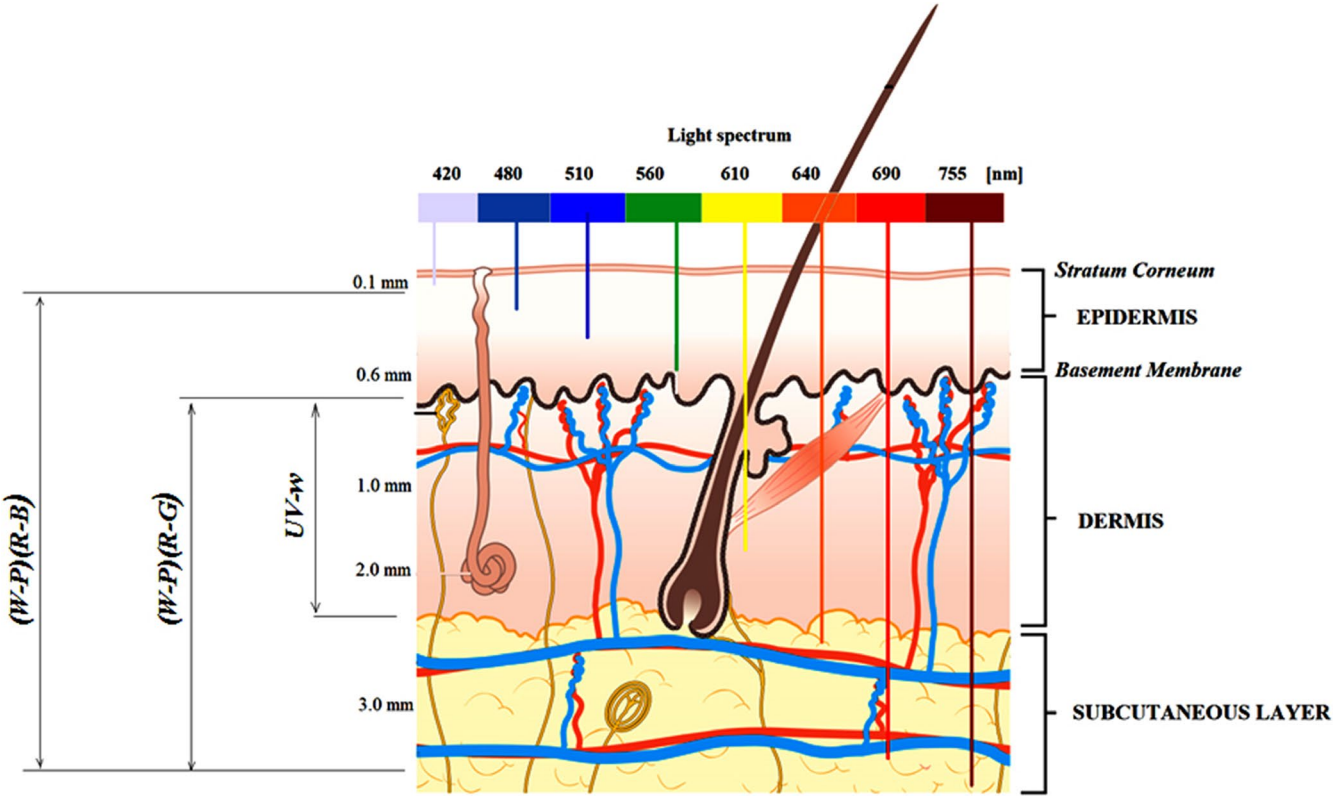

FIGURE 4 Characterization of the skin biophysical state with OMIS method based on penetration depth defined with specific wavelengths (adapted from [17,21,26])

because p^+/p^- is changed from 1.79 to 0.64 in (W-P)(R-B) spectra, which means that electrons are more paired. After the treatment with *body lotion with 3HFWC*, collagen-water interaction in dermis becomes more dynamic, because p^+/p^- in (W-P)(R-G) spectrum increases from 0.82 to 0.97. However, skin tissue, both epidermis and dermis, becomes more compact (stable) because p^+/p^- in (W-P)(R-B) spectrum is changed from 0.92 to 0.80, indicating that electrons have become paired. After the treatment with *hand cream with 3HFWC* collagen-water interaction becomes more stable (dynamics of p^+/p^- in (UV-w), spectrum is around 0.49, which represents its equilibrium. Also, the skin tissue in general becomes stable because p^+/p^- in (W-P)(R-B) spectrum is changed from 0.78 to 0.52, indicating that electrons have become paired.

Base cream—*Vehiculum of body lotion* shows statistically significant improvement based on the (W-P)(R-B) and (UV-w) parameters. The increase in the number of paired electrons and diamagnetic properties indicates higher density of the skin tissue under the stratum corneum and better signal transfer through collagen-water interactions (UV-w). While vehiculum does not have influence on the lower layer of the skin—dermis, (W-P)(R-G), it can change the state of the upper level of the skin. Compared to the *body lotion with 3HFWC*, which improves state of the fiber molecules in the dermis, mostly collagen, *vehiculum with water of body lotion* can accelerate the signal transfer in the upper level of the skin and provoke faster reaction to the negative external and internal influences. *commercial hand cream* has the opposite effect compared to the *body lotion*—this cream has positive influence on the dermis, while *hand cream with the 3HFWC* acts on the upper level of the skin. *Commercial hand cream* has the effect of increasing the diamagnetic properties (less unpaired electrons) and improving the compactness of the dermis.

Difference between the p^+/p^- parameters that showed statistical significance before the treatment and after the treatment obtained for different creams with different types of light ((W-P)(R-B), (W-P)(R-G), (UW-w)) ranges from 0.09 to 2.78 (Table 2). However, for all skin structures (skin surface, epidermis, and dermis) average difference value ranges from 12% to 32%.

5 | DISCUSSION

Patented hyper-harmonized-hydroxylated fullerene water complex (3HFWC) used in this study demonstrated positive effects on quality, as well as, on quantity of collagen fibers and improvement of the basement membrane functionality. Depending on the type of the cream, the average improvement is 22.5%, based on arithmetic value of 12% (body lotion), 18% (regenerating cream), 28% (antiaging), and 32% (hand cream).

The 3HFWC structure with the formula $C_{60}(OH)_x@(H_2O)_y$ is extremely rich with OH groups, and cloud of crystalline water surrounding the basic structure—fullerene-C_{60}. Fullerols are ingredients with unique paramagnetic/diamagnetic properties. They are structured

TABLE 2 Significant results obtained by statistical analysis using paired *t* test for the comparison of p^+/p^- values before and after the treatment with cosmetic products with 3HFWC, commercial creams, and vehiculum

Cosmetic product	Type of cream	Criterion	p^+/p^- Before the treatment	p^+/p^- After the treatment	*t* test *P* value*
Regenerating cream	Vehiculum	(W-P)(R-B)	1.15	1.2	*
		(W-P)(R-G)	0.89	0.66	*
		UV-w	0.53	0.74	*
	Commercial	(W-P)(R-B)	1.01	1.02	*
		(W-P)(R-G)	0.69	0.72	*
		UV-w	0.53	0.6	*
	+3HFWC	(W-P)(R-B)	0.68	0.78	0.03
		(W-P)(R-G)	0.83	0.76	0.013
		UV-w	0.56	0.55	*
Anti-aging cream	Vehiculum	(W-P)(R-B)	0.92	1.12	*
		(W-P)(R-G)	0.9	0.89	*
		UV-w	0.62	0.73	*
	Commercial	(W-P)(R-B)	0.68	0.81	*
		(W-P)(R-G)	0.98	0.72	*
		UV-w	0.51	0.62	*
	+3HFWC	(W-P)(R-B)	1.79	0.64	<0.0001
		(W-P)(R-G)	0.86	0.95	*
		UV-w	0.74	0.51	<0.0001
Body lotion	Vehiculum	(W-P)(R-B)	0.2	1.03	0.0001
		(W-P)(R-G)	0.74	0.92	*
		UV-w	0.3	0.55	0.01
	Commercial	(W-P)(R-B)	0.59	1.07	*
		(W-P)(R-G)	0.96	0.69	*
		UV-w	0.39	0.57	*
	+3HFWC	(W-P)(R-B)	0.92	0.81	*
		(W-P)(R-G)	0.82	0.97	0.002
		UV-w	0.51	0.56	*
Hand cream	Vehiculum	(W-P)(R-B)	0.67	0.93	*
		(W-P)(R-G)	0.74	0.85	*
		UV-w	0.59	0.57	*
	Commercial	(W-P)(R-B)	0.95	0.76	*
		(W-P)(R-G)	0.28	0.85	0.003
		UV-w	0.51	0.47	*
	+3HFWC	(W-P)(R-B)	0.78	0.52	<0.0001
		(W-P)(R-G)	0.78	0.84	*
		UV-w	0.63	0.49	<0.0001

*$P > 0.05$, results are not statistically significant.

by Fibonacci sequences, the Golden Mean law, and the vibrations of these molecules can pass to hydrogen bonds of ubiquitous water molecules and reorganize the unnatural state of biomolecules, forcing them to oscillate in the natural way.[16,17] Material with paramagnetic feature will boost magnetic field and upgrade the arrangement of dipole molecules, like water and proteins molecules.[18,22] This arrangement of biomolecules improves dynamic properties and signal transduction, and thus, the skin can react faster to the information from the inside and outside and regenerate better. These effects are very important for the treatment of aged skin, skin subjected to the hostile environmental factors, and exposed to inadequate way of life and skin care.

Changes of paramagnetic/diamagnetic properties can be obtained by the (UV-w) criterion. An increase of paramagnetic properties and number of unpaired electrons enable collagen molecules to transfer signals and information. Results in Table 2 show that

Anti-Aging Cream with 3HFWC ($P < 0.0001$), *hand cream with 3HFWC* ($P < 0.0001$), and *vehiculum of body lotion* ($P = 0.01$) have significantly increased paramagnetic properties. The tissue demonstrates better dynamic properties and electric charge, that is signals move faster.

Under the influence of environmental or some other factors, molecules and their vibrations can be changed and normal behavior of collagens can be disrupted. In that case, function of the basement membrane is impaired, and many cells in basal layer of epidermis cannot get supplies. From esthetic point of view, slower keratinization and regeneration processes in the skin can occur as well as aged appearance. According to the (W-P)(R-B) criterion, statistically significant improvements were detected in the case of *Regenerative Cream with 3HFWC* ($P = 0.03$), *Anti-aging Cream with 3HFWC* ($P < 0.0001$), *hand cream with 3HFWC* ($P < 0.0001$), and *vehiculum of body lotion* (Table 2), indicating that these products have an impact on epidermal layer and basement membrane. Based on the previous experimental research on collagen-C_{60} interaction and new data in this field, the authors assume that 3HFWC, as an improvement of the earlier substance, has a possibility to harmonize disrupted oscillatory process between collagen type I and III (horizontal oscillations) and collagen type IV and VII (vertical oscillations).[9,16,18] Using biophysical and not biochemical approach, the authors strongly believe that 3HFWC improves function and firmness of the basement membrane and that it could give better quality and appearance of the skin.

According to the previous investigations, proper order of biomolecules in the epidermis can induce better function of fibroblasts in the dermis and enforce fiber protein synthesis.[16,18] Repaired structure of collagen molecules transforms information better, provokes regeneration of existing and synthesis of new collagen molecules. Results obtained with the (W-P)(R-G) criterion (Table 2) show statistically significant improvements in abundance and quality of collagen in extracellular matrix of the dermis with *regenerating cream with 3HFWC* ($P = 0.013$) and *body lotion with 3HFWC* ($P = 0.002$). Commercial hand cream gave similar results ($P = 0.003$) for (W-P)(R-G) criterion. *Hand cream with 3HFWC* demonstrated the improvement of skin structure in both dermis and epidermis as well as of basement membrane ((W-P)(R-B) criterion), but at the same time the increase of paramagnetic properties (better signal transduction through collagen molecules). When the transfer of the signals through the skin is faster, the faster reaction and better protection of the skin from negative influences from the outside is expected.

6 | CONCLUSION

In order to understand quantum properties of biomolecules (its conformation changes) and tissues/organs functionality in human body better, corresponding devices and methods that enable their measurements were used. One of them is OMIS method, which was successfully used in skin, cervix, and colon cancer detection.[23-25] Since OMIS method is very sensitive to conformation changes in biomolecules, it enabled the demonstration of improvements of biophysical properties and collagen molecules in the skin after the treatment of the skin with cosmetic products containing 3HFWC. Compared to the commercial products and vehiculums, all cosmetic products with 3HFWC except body lotion have shown significant improvements of the functionality of basement membrane. While *regenerating cream* and *body lotion with 3HFWC* have positively affected collagen quality in the dermis, *Anti-aging* and *hand cream with 3HFWC* have shown positive effects on signal transduction and regeneration of collagen. Results imply that *Anti-aging* and *hand cream with 3HFWC*, as well as *body lotion vehiculum*, could improve properties of basement membrane and accelerate signal transduction in the dermis, and finally enable faster regeneration of the epidermis and rapid reaction of the skin to the negative environmental influences. *Regenerating cream with 3HFWC* has shown positive effects on the basement membrane and strength of the collagen supportive structure in the skin. The *body lotion with 3HFWC* and *commercial hand cream* have improved mechanical properties of the skin through strengthening the collagen fibers in the dermis. The ingredient—3HFWC, which acts in natural, biophysical way on the skin, might open new era in the way we understand and treat changes in the altered and aging skin.

ACKNOWLEDGMENT

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ETHICAL APPROVAL

The study follows the tenets of the Declaration of Helsinki.

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