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Efficacy Evaluation of a Natural Synergy of Botanical Extracts to Improve Skin Beauty

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Abstract

Purpose: The present study was aimed at evaluating the efficacy of a natural nutraceutical ingredient in reducing the skin imperfections of the face and the body.

Patients and methods: A randomized, double-blind, placebo-controlled study was carried out on 66 subjects Caucasian females aged between 35 and 65 years old showing the following clinical signs: with fine lines/slightly visible wrinkles, dull skin and uneven skin tone, dark circles, eye bags, and mild to moderate cellulite-derived skin imperfections. Product efficacy was assessed by means of both non-invasive skin bioengineering techniques and anthropometric measurements. The instrumental measurements were integrated by clinical analysis carried out by a board-certified dermatologist and by a self-assessment questionnaire carried out by each subject participating in the study.

Results: We reported a positive effect of the product intake both on facial and body skin imperfection. The product intake for 56 days was effective in improving the skin surface parameters, the skin moisture content, the skin radiance, the eyebags/dark circles appearance, the waistline/hips/thighs circumferences, and the cellulite-induced alteration to skin microcirculation.

Conclusion: The oral supplementation with the test product represents a useful approach to address the multifactorial discomfort that is generically identified as skin imperfection.

Keywords: ***Natural botanical extract; Black rice seed extract; Kiwi dried powder; Orange extract; Pineapple extract; Skin imperfections***

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1. Introduction

The global beauty market is undergoing an extremely high growth in recent years and many beauty products have been developed with the aim to ensure the maintenance of the normal physiological aspect of the skin and improve its general smoothness [1,2]. Having a good skin quality is of the utmost importance nowadays since it significantly influences many aspects in people lives such as the perception of age, attractiveness, health, and youth [3].

In fact, as the largest organ of the body, skin represents the first defense line against the external environment [4,5]. It has multiple key roles in the sensitivity and protection towards physical, chemical, and biological aggressors of the human body and it helps maintain the correct homeostasis of the organism [5,6]. The loss of structural and functional integrity of the skin contributes to the occurrence of skin lesions, which can in turn lead to dermatological problems affecting skin health and appearance [7].

Exogenous stressors, such as UV rays or pollutants, but also physiological changes induced by the progress of time can impair skin tone leading more in general to a reduced quality of the skin [8]. For these reasons, firmness, glow, evenness of surface and tone are the main parameters to take into account when assessing skin quality, for both face and body, in order to ensure a good skin tonicity, brightness and uniformity which are important not only for health, but also for the emotional wellbeing of the individual [7].

Under eye bags and dark circles represent two of the most frequent types of skin imperfections on the face: the former result from the accumulation of loose skin and from the reduction of muscle volume, both of which occur with age [9]; the latter are bilateral, round, homogeneous pigment macules on the infraorbital regions [10]. These anti-aesthetic conditions affect individuals of all ages and impart a fatigued and less youthful appearance to the face [11]. Although there is no doubt that such imperfections are worsened by general fatigue, especially lack of sleep, they are linked to many physiological and environmental factors and, for this reason, the specific etiology and therapy are not fully understood [10,12]. Nevertheless, it remains clear that such conditions can affect an individual's mental and physical wellbeing and influence the quality of life [12].

Skin imperfections of the whole body are also a common target of many beauty products, and their prevalence is particularly high among women. Cellulite is one of the major anti-aesthetic skin conditions affecting 80% to 98% of post pubertal women [13]. It is characterized by the typical "orange-peel" appearance, and it is usually found on thighs and buttocks [13-16]. Its occurrence is linked to many different factors: structural, inflammatory, morphologic, and biochemical alterations in the subcutaneous tissue are the main key players for cellulite development, but also hormonal imbalances linked to estrogens activity can explain the higher prevalence among women [16]. In addition, microvascular dysfunction is considered a predisposing factor for cellulite onset [14]: in the area affected by cellulite, in fact, the blood flow is estimated to be 35% lower than in non-affected regions [17] and for this reason, skin irregularities are more prone to appear in areas in which circulation and lymphatic drainage is decreased, such as the buttocks and thighs [14]. Therefore, several anti-cellulite ingredients have been developed to improve skin microcirculation and to reduce the "orange peel" appearance [17].

Besides the usual cosmetic treatments against cellulite, much attention has recently increased towards nutricosmetics, a concept that derives from the intersection of cosmeceutical and nutraceutical, and which often refers to natural health products, taken as food supplement, able to enhance the function and appearance of skin, hair, and nails, thus generating a cosmetic benefit [18]. Thanks to the development of the so-called "*beauty supplements*", it combines the benefits derived from food supplementation with the advantages of cosmetic treatments, thus helping to protect skin and improve its quality and appearance [19].

In a first randomized, double blind and placebo-controlled clinical study on healthy women, the oral supplementation with SelectSIEVE® Rainbow, based on four different botanical extracts, was found to be effective in achieving a good body-shaping activity together with a reduction in subcutaneous fat mass and a general improvement in microcirculation, thus reducing cellulite imperfections [20]. The mixture showed strong anti-inflammatory, antioxidant, proteolytic and hypolipidemic activity *in vitro*, resulting from the individual and peculiar properties of components as well as from their synergic effects. Black rice, is well-known for its high content of flavonoids, among which anthocyanins [21,22], effective on microcirculation and lymph drainage [23,24] and with an anti-obesity effect, due to their adipocytokines modulatory activity exerted on adipocytes [25,26]; orange fruit, has an antioxidant effect due to its vitamin C content, but it also contains anti-inflammatory compounds useful for the treatment of metabolic dysregulation [27,28]; bromelain, from pineapple stems, is a mixture of proteolytic enzymes with anti-inflammatory activity and effective in reducing swelling [29,30]; and kiwifruit, that besides being a source of vitamin C, it also contains polysaccharides with a stimulating activity on fibroblasts and keratinocytes proliferation thus leading to an increase in skin metabolic activity [31,32].

Considering this evidence, the present study was carried out in order verify the efficacy of the administration of SelectSIEVE® Rainbow on a different skin district, the face, which, in terms of women beauty, represents the area that deserves the highest attention due to the continuous exposure to noxious agents (exposome). Facial skin profilometry was assessed in terms of wrinkledness, moisturization, brightness, and homogeneity; furthermore, skin evenness, skin pinkish, under eye bags volume and dark circles appearance, were also considered. Concurrently, the efficacy of the treatment in reducing the cellulite-derived skin imperfections ("orange peel" appearance), thus improving skin microcirculation, was evaluated in the panel of women to confirm the results from the previous study.

2. Material and Methods

2.1 Description of study design and study flow

This multi-center, randomized, double-blind, placebo-controlled, parallel group clinical study was carried out at Complife Italia Srl facilities in Milan and in Biella. The trial was carried out in compliance with the Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amendments). Both the study protocol and the informed consent form were approved by the "Independent Ethical Committee for Non-Pharmacological Clinical trials", Genova, Italy (ref. 2022/09). All participants were fully informed of the study risks and benefits, aims and procedures and they provided a written Informed Consent Form (IFC) as well as a signed consent release form for the publication of photographs prior to the attendance to the study. Study was registered at ISRCTN registry (Registration number: ISRCTN36901382, https://doi.org/10.1186/ISRCTN36901382).

Enrolled subjects attended three clinic visits at baseline (T0) and after 28 (T28) and 56 (T56) days of product use. At T0 subjects were measured (clinical and instrumental evaluations), received the test products, a daily diary, and instructions about the trial procedures. At T28 and T56 the compliance of subjects with treatment was checked by product accountability.

2.2 Eligibility criteria for participants

The study enrolled sixty-six females. Eligible participants were all healthy adult Caucasian females aged between 35 and 65 years old (extremes included) who met the following inclusion criteria: phototype I to IV included (Fitzpatrick classification, fine lines/slightly visible wrinkles, dull skin and uneven skin tone, dark circles (10 subjects per group), eye bags (10 subjects per group), mild to moderate cellulite-derived skin imperfections; subjects who have not been involved in any other similar study in the last 3 months; subjects able to respect the instructions given by the investigator as well as able to respect the study constraints and specific requirements; commitment not to change the daily routine or the lifestyle. The study excluded subjects not meeting the inclusion criteria, breastfeeding, pregnant or not willing to take necessary precautions to avoid pregnancy during the study (for the women of childbearing potential), acute/chronic skin or systemic disease able to interfere with the outcome of the study or that are considered dangerous for the subject or incompatible with the study requirements; participation or planning to participate in other clinical trials, acute/chronic/progressive illness liable to interfere with the study data or considered by the Investigator hazardous for the subject or incompatible with the study requirements; pharmacological treatments that are considered incompatible with the study requirement by the investigator; allergies or sensitivity to food supplements and cosmetic products.

2.3 Intervention

The active product was a food supplement containing 300 mg of SelectSIEVE® Rainbow (Roelmi HPC, Origgio, Italy), a mixture of botanical extracts with the following composition: Black rice seed extract (*Oryza sativa L. Semen*) 35%-45% w/w; Kiwi dried powder (*Actinidia chinensis Planch Fructus*) 30%-40% w/w; Orange extract (*Citrus sinensis L. Osbeck Fructus*) 20%-30% w/w; Pineapple extract enriched with Bromelain (*Ananas comosus (L.) Merr*) 1%-5% w/w; 19 mg of Maltodextrin; 31 mg of Vegetal Magnesium Stearate, 95 mg of CPS HPMC. In the placebo capsules SelectSIEVE® Rainbow was substituted by maltodextrin and purple dye to achieve the same colour of the active capsules.

SelectSIEVE® Rainbow and Placebo capsules were manufactured in accordance with the guidelines and regulations applicable in the field (food regulation). Subjects were instructed to intake one capsule/day of food supplement or placebo with a glass of still water for 56 days.

Each enrolled volunteer was also provided with a face/body cream, without any cosmetic active ingredient, to be used during the whole study period instead of their day/night face cream and body cream. The ingredient list of the face/body cream is as follows: AQUA, TRIPELARGONIN, NEOPENTYL GLYCOL DIPELARGONATE, POLYGLYCERYL-3 STEARATE, TRIOLEIN, C10-18 TRIGLYCERIDES, CETEARYL ALCOHOL, GLYCERYL DIOLEATE, SUNFLOWER SEED OIL GLYCERIDES, HYDROXYETHYLCELLULOSE, CAPRYLYL GLYCOL, ETHYLHEXYLGLYCERIN, O-CYMEN-5-OL, PARFUM.

2.4 Primary and secondary objectives and outcome measures

Primary objective of the study was to investigate the efficacy of the treatment in improving face skin condition by both clinical assessment (skin evenness complexion, skin pinkish, eye bags and dark circles appearance) and instrumental measurements (dark circles colour analysis, skin deep moisturization, skin brightness, and skin profilometry).

Secondary objective of the study was to investigate the reduction of cellulite-derived imperfections of the body were concurrently evaluated in the panel by both clinical assessment (skin smoothness, "orange peel" skin appearance, skin microcirculation) and instrumental measurements (skin profilometry, body weight, and body circumferences). Digital pictures were taken through the study for both face and body clinical evaluations.

A self-assessment questionnaire about the perceived efficacy of the treatment was filled by the participant at T28 and T56. All the clinical and instrumental parameters were assessed by a dermatologist under controlled room conditions (T=22°C ± 2°C and RH=50% ± 10%) after 15-20 minutes of acclimatization.

2.4.1 Skin profilometry

The skin surface characteristics of both the face (periocular area) and the thighs were measured using a real 3D camera (Primos^{CR} SF, Canfield Scientific Europe, BV, Utrecht, Netherlands) based on structured light projection. The following parameters were measured: the skin roughness Ra and Rz parameters were measured to assess the product efficacy in improving the skin smoothness of the periocular area ("crow's feet" wrinkles), the volume was measured to assess the product efficacy in decreasing eye bags appearance, and the skin roughness Ra parameter was measured to assess the product efficacy in improving the skin smoothness of the thigh.

2.4.2 Deep skin moisturization

The deep skin moisturization was measured in the cheeks by MoistureMeterEpiD (Delfin Technologies Ltd, Kuopio, Finland), an all-in-one measurement unit (an integrated probe, a built-in contact force sensor and a display) that by generating a high frequency, 300 MHz, and low power electromagnetic (EM) wave to the portion of the exposed skin shows a non-invasively measurement of the percentage values of local tissue water.

2.4.3 Colorimetric measurements

The skin colour and radiance characteristics were measured using a spectrophotometer/colorimeter CM-700D (Konica Minolta, Milan, Italy). This instrument measures the colour in the standardized CIELab chromatic space. The 8° gloss parameter was measured to assess the skin radiance (e.g., the ability of the skin to reflect the light) and the L* and b* parameters were measured to calculate the individual typology angle (ITA°) as an index of the colour intensity of the dark circles.

A low ITA° value indicates a dark colour while a high ITA° value indicates a very light pigmentation.

2.4.4 Anthropometric measurements

Measurement of body weight and height was carried out with the subject barefooted and wearing underwear using an electronic balance and a stadiometer, respectively. Body circumferences (waistline, thigh, and hips) were measured using a flexible meter (precision: 1 mm). The waistline circumference was measured just above the right and left iliac crest, the hip circumference and thigh circumferences were measured in their maximum protrusion.

2.4.5 Assessment of cellulite-induced alteration of skin microcirculation

The efficacy of the product in improving the cellulite-derived blood and lymphatic microcirculation alterations were measured by clinical scoring on the thermal images of the thighs taken using a FLIR E95 thermal camera (Teledyne FLIR LLC, Oregon, US), as follows: 1 no improvement, 2 mild improvement, 3 moderate improvement, 4 strong improvement.

2.4.6 Clinical evaluation

The improvement of skin evenness complexion (face), eye bags and dark circles appearance, and "orange peel" appearance was scored out according to the following internal clinical scale: 1 no variation, 2 mild improvement, 3 moderate improvement, 4 strong improvement. Skin pinkish (face) was evaluated through a VAS scale, with score from 0 (absence of red, i.e., pinkish aspect) to 10 (red aspect).

2.4.7 Digital pictures

Digital pictures of the face were taken, throughout the study, by means of Visioface (Courage + Khazaka electronic GmbH, Köln, Germany) that ensures a reproducible subject positioning between timepoints and take pictures using standard light conditions. Digital pictures of the body (cellulite affected areas) were taken using a digital reflex camera (Nikon D610, Nital S.p.A., Moncalieri, Italy) under standard lighting conditions.

2.4.8 Self-assessment questionnaire

After 28 and 56 days of treatment, subjects were asked to express their opinion on the treatments by answering to a questionnaire about products effects and acceptability. Threshold percentage for positive answers was set at 60% of the subjects.

2.5 Statistical analysis

An appropriate statistical model (parametric or not parametric) was applied based on data distribution. For each parameter under study Intra-group statistical analysis (T28 vs T0; T56 vs T0) and Inter-group statistical analysis (active vs. placebo) were carried out. A p values <0.05 was considered as statistically significant. An appropriate statistical model was chosen as follows: RM-ANOVA followed by Tukey-Kramer post hoc test for repeated measures and normally distributed data; Friedman test followed by Tukey-Kramer post hoc test for repeated measures and not normally distributed data; 2-way Student's test t for unpaired data for inter-group statistical analysis. The statistical software used to generate the randomization list was PASS 11

(version 11.0.8; PASS, LLC. Kaysville, UT, USA). The statistical software used for statistical analysis was: NCSS 10 (version 10.0.7 for Windows; NCSS, Kaysville, UT, USA).

3. Results

3.1 Participants

Seventy-eight (n=78) subjects were screened for eligibility; out of them 9 did not meet the inclusion criteria and 3 declined to participate (FIG. 1). The study randomized, then, 66 subjects; 33 subjects were allocated to the active treatment arm and 33 subjects were allocated to the placebo treatment arm. The per protocol (PP) population consisted of 61 subjects. In the active group the study was finished by 31 subjects while 30 subjects finished the study in the placebo group. The reason for not being included in the PP population were one of the following: withdrew due to personal reason (n=2 in the placebo group and n=1 in the active group), occurrence of a sensation of abdominal swelling (n=1 in the placebo group) and worsening of a pre-existing condition of constipation (n=1 in the active group). The mean age (mean ± SE) was 50.5 ± 1.3 in the active group and 49.1 ± 1.6 in the placebo group. Others demographic data at inclusion are reported in TABLE 1.

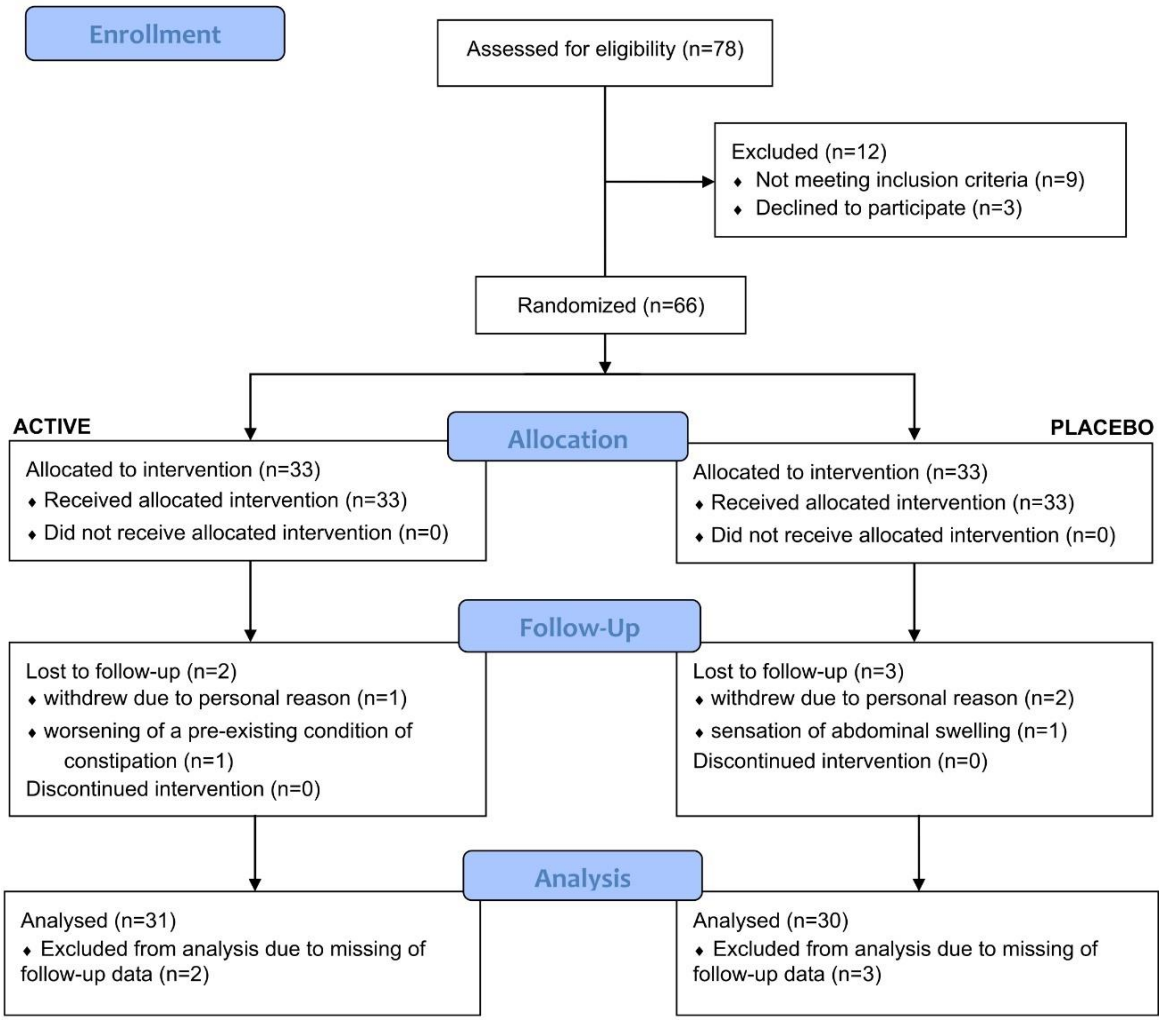

FIG. 1. **SelectSIEVE® Rainbow flow diagram.**

TABLE 1. **Demographic data and baseline characteristics. Data are means ± SE. In bracket is reported the percentage of subjects. n.a. not applicable; a.u. arbitrary units. BMI Body Mass Index. * p<0.05, ** p<0.01, *** p<0.001.**

	Active (n=31)	Placebo (n=30)	p-value[1]	Units
Sex				
Female	31 (100%)	30 (100%)	n.a.	N (%)
Male	0 (0%)	0 (0%)	n.a.	
Age	50.5 ± 1.3	49.1 ± 1.6		Years
Anthropometric parameters				
Body weight	64.8 ± 1.7	62.2 ± 1.5	0.2442	Kg
BMI	25.0 ± 1.6	23.7 ± 0.5	0.1058	$Kg \cdot m^{-2}$
Waistline circumference	83.9 ± 1.7	82.0 ± 1.6	0.4232	cm
Thigh circumference	57.9 ± 1.2	55.5 ± 0.7	0.095	cm
Hips	100.7 ± 2.1	98.3 ± 1.4	0.366	cm
Skin profilometry				
Ra (face)	34.26 ± 0.93	33.74 ± 1.26	0.7372	□m
Ra (thigh)	30.86 ± 0.95	31.17 ± 1.32	0.1962	□m
Rz (face)	209.62 ± 6.97	196.88 ± 6.55	0.1886	□m
Eye bags volume	14.10 ± 1.72	14.71 ± 0.77	0.7771	mm^3
Colorimetric measurement				
8° gloss	10.2 ± 0.4	10.7 ± 0.4	0.3997	a.u.
ITA°	28.46 ± 1.39	27.82 ± 1.37	0.7473	a.u.
Deep skin moisturization	36.5 ± 1.2	37.0 ± 1.3	0.7647	%

[1] two-way unpaired test of Student.

3.2 Skin profilometry

The active treatment determined a progressive and statistically significant (p<0.001) intragroup reduction of Ra and Rz parameters in the periocular area, as follows: -7,5% at T28, and -12,1% at T56 for Ra and -6,9% at T28, and -10,8% at T56 for Rz (FIG. 2a/c). A slight and significant reduction of both parameters was recorded also in the group receiving the placebo treatment; however, such reduction was recorded only at T56, and was as follows: -2.2% (p<0.05) for Ra and -4.0% (p<0.01) for Rz. Differences between the active and the placebo treatment were statistically significant (p<0.01 at T28 and p<0.001 at T56 for both Ra and Rz parameters).

The Ra parameter measured in the thigh area was also statistically significant decreased in the active treatment arm as follows: -7.6% and -11.1%, at T28 and T56, respectively (FIG. 2b). A slight but not statistically significant reduction was recorded also in the group receiving the placebo treatment. Differences between the active and the placebo treatment were statistically significant both at T28 (p<0.001) and T56 (p<0.001).

Both the active and the placebo treatment resulted in a progressive and statistically significant intragroup reduction of eye bags volume vs. baseline as follows: -4.9% (p<0.01) in the placebo group vs. -6.2% (p<0.05) in the active group at T28 and -6.5% (p<0.001) in the placebo group vs. 9.1%(p<0.01) in the active group at T56 (FIG. 2d). However, no statistically significant

intergroup differences were reported at T28 and T56. The instrumental result was also confirmed by the clinical analysis. Visually, at T56 in the active group the clinical analysis showed an improvement of the eye bags appearance in most of the enrolled subjects (50.0% active vs. 12.5% placebo). At T28 an improvement of the eye bags appearance was seen in less than the 50% of the subjects.

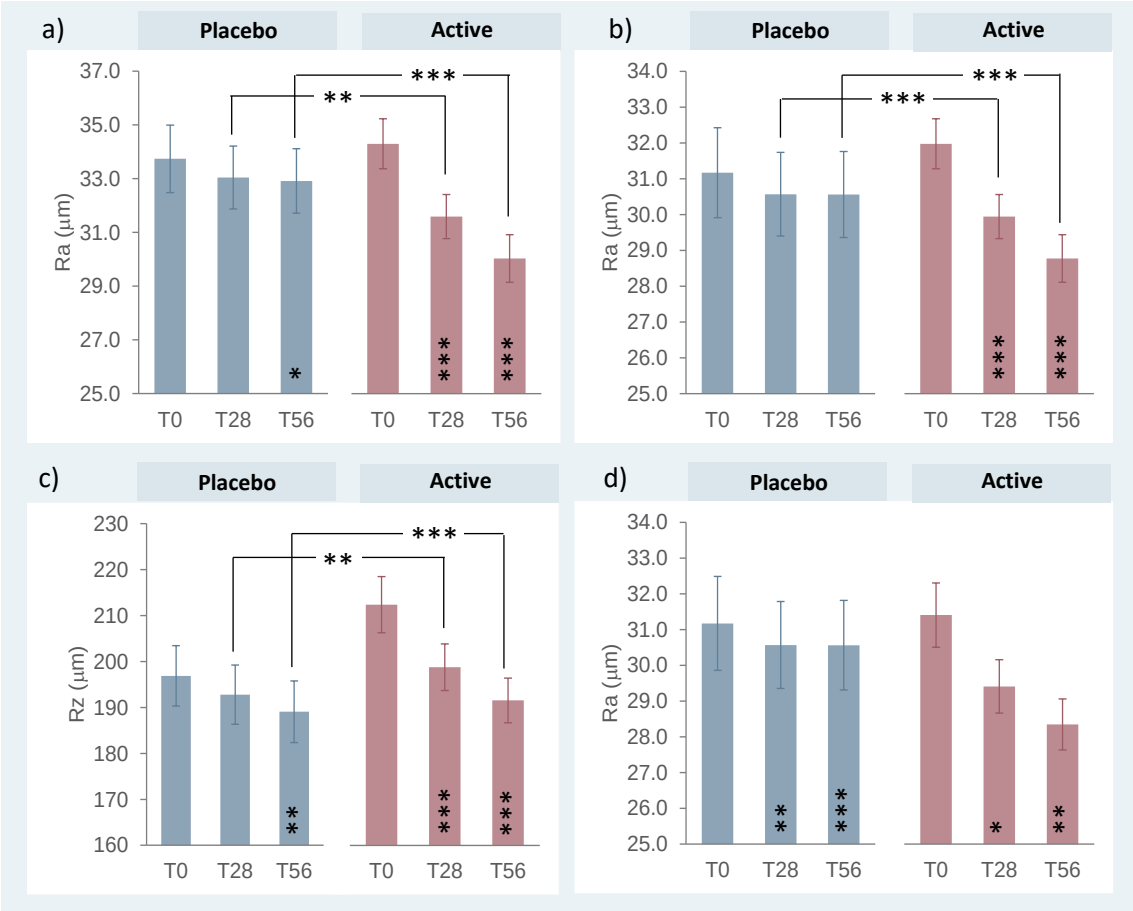

FIG. 2. **Skin profilometry results. a) Ra parameter in the periocular area. b) Ra parameter in the thigh area. c) Rz parameter in the periocular area. d) Eye bags volume. Data are mean ± SE. The intragroup statistical analysis is reported inside the bars while the intergroup statistical analysis is reported above the bars (blue lines). * p<0.05, ** p<0.01, *** p<0.001. Placebo Active.**

3.3 Deep skin moisturization

In the active treatment arm, the epidermis water content was statistically significantly increased as follows: +5.9% ($p<0.01$) and +9.5% ($p<0.001$) at T28 and T56, respectively (FIG. 3). A slight and statistically significant improvement of the water amount contained in the epidermidis was recorded also in the placebo group, however such increment was registered only at T56, and it accounted for only +3.0% ($p<0.05$). Differences between the active and the placebo treatment were statistically significant both at T28 ($p<0.05$) and T56 ($p<0.01$).

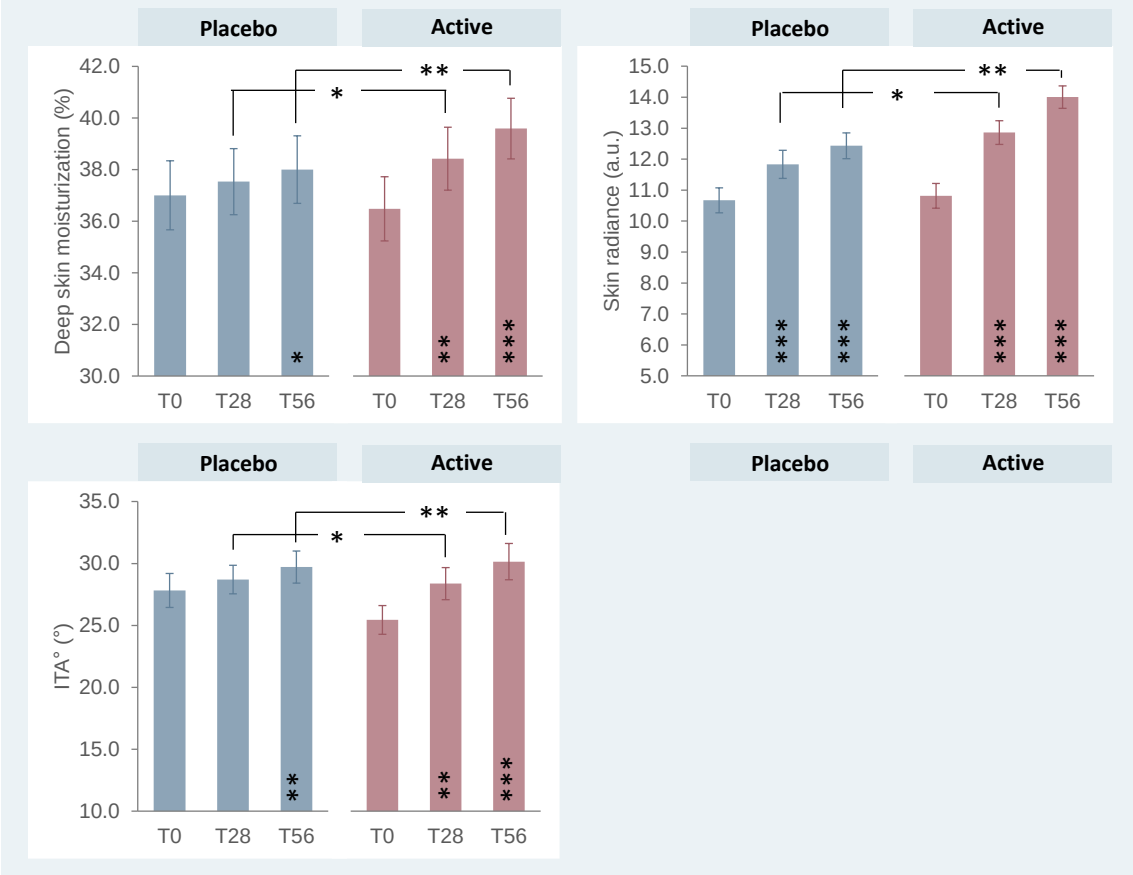

FIG. 3. **Product effect on skin. a) Deep skin moisturization. b) Skin radiance (8° gloss). c) Intensity of dark circles (ITA°). Data are mean ± SE. The intragroup statistical analysis is reported inside the bars while the intergroup statistical analysis is reported above the bars (blue lines). * p<0.05, ** p<0.01, *** p<0.001. Placebo Active. a.u. arbitrary units.**

3.4 Colorimetric measurements

Both the active and the placebo treatment resulted in a progressive and statistically significant (p<0.001) intragroup increment of the mean value of gloss parameter, respectively +11.2% in the placebo group and +19.9% in the active group at T28, and 17.5% in the placebo group and +30,4% in the active group at T56. Differences between the active and the placebo treatment were statistically significant both at T28 (p<0.05) and T56 (p<0.01).

The active treatment resulted in a progressive and statistically significant intragroup increment of the ITA° value as follows: +12.6% (p<0.01) at T28 and +19.9% (p<0.001) at T56. A progressive improvement of ITA° value was recorded also in the group receiving the placebo treatment, however such increment resulted statistically significant only at T56, accounting only for +7.2% (p<0.01). Differences between the active and the placebo treatment were statistically significant both at T28 (p<0.05) and T56 (p<0.01). Visually, at T56 in the active group the clinical analysis showed an improvement of the eye bags appearance

in most of the enrolled subjects (75.0% active vs. 33.3% placebo). At T28 an improvement of the eye bags appearance was seen in less than the 50% of the subjects.

3.5 Clinical evaluation

A statistically significant pinkish effect was seen at T28 (45.5% of the subjects, $p<0.05$) and T56 (64.5% of the subjects, $p<0.001$) in the active group. A positive effect, in the placebo group, was seen only at T56 (40.0% of the subjects, $p<0.001$). The active treatment resulted in a clinically relevant improvement of skin evenness complexion at T56 as it was recorded in 67.7% of subjects (vs. 26.7% of the subjects in the placebo treatment arm). Placebo and active treatment showed an improvement in <50% of subjects at t28.

The active treatment resulted in a clinically relevant decrease of the "orange peel" skin appearance at T56 in 64.5% of subjects, while <50% of subjects that received the placebo or the active treatment at T28 registered an improvement.

3.6 Anthropometric measurements

Both the active and the placebo treatment did not result in a statistically significant body weight variation (TABLE 2). A statistically significant ($p<0.05$) variation between was seen between the active and the placebo group.

TABLE 2. **Anthropometric results. Data are means ± SE. In bracket is reported the percentage of variation vs. T0 (baseline). BMI Body Mass Index.**

		T0	T28	T56
Weight (Kg)	Placebo	62.2 ± 1.5	62.2 ± 1.5 (0.0)	62.2 ± 1.5 (0.0)
	Active	64.8 ± 1.7	64.4 ± 1.7 (-0.4)	64.2 ± 1.7 (-0.6)*
BMI (Kg·m^{-2})	Placebo	23.7 ± 0.5	23.7 ± 0.5 (0.0)	23.7 ± 0.5 (0.0)
	Active	25.0 ± 0.6	24.8 ± 0.6*** (-0.2)	24.8 ± 0.6** (-0.2)*
Waistline circumference (cm)	Placebo	82.0 ± 1.6	81.7 ± 1.6 (-0.3)	81.7 ± 1.7 (-0.3)
	Active	83.9 ± 1.7	83.2 ± 1.7*** (-0.6)*	82.9 ± 1.6*** (-1.0)**
Hips circumference (cm)	Placebo	98.3 ± 1.4	98.0 ± 1.4 (-0.3)	98.0 ± 1.4 (-0.3)
	Active	100.7 ± 2.1	100.0 ± 2.1*** (-0.7)*	99.8 ± 2.1*** (-0.9)*
Thigh circumference (cm)	Placebo	55.5 ± 0.7	55.5 ± 0.7 (0.0)	55.4 ± 0.7 (-0.1)
	Active	57.9 ± 1.2	57.5 ± 1.2*** (-0.4)*	57.1 ± 1.1*** (-0.8)***

The active treatment resulted in progressive and significant ($p<0.001$) intragroup reduction of waistline circumference as follows: -0.6 cm and -1.0 cm at T28 and T56, respectively. No significant reduction of thigh circumference was recorded also

in the group receiving the placebo treatment. Differences between the active and the placebo treatment were statistically significant both at T28 ($p<0.05$) and T56 ($p<0.01$).

The active treatment resulted in progressive and significant ($p<0.001$) intragroup reduction of hips circumference as follows: -0.7 cm and -0.9 cm at T28 and T56, respectively. No significant reduction of thigh circumference was recorded also in the group receiving the placebo treatment. Differences between the active and the placebo treatment were statistically significant both at T28 and T56 ($p<0.05$).

The active treatment resulted in progressive and significant ($p<0.001$) intragroup reduction of thigh circumference as follows: -0.4 cm and -0.8 cm at T28 and T56, respectively. No significant reduction of thigh circumference was recorded also in the group receiving the placebo treatment. Differences between the active and the placebo treatment were statistically significant both at T28 ($p<0.05$) and T56 ($p<0.001$).

3.7 Assessment of cellulite-induced alteration of skin microcirculation

Thermographic evaluations of the skin microcirculation revealed that the active treatment resulted in a clinically relevant improvement of skin microcirculation at T56 as it was recorded in 58.1% of subjects, whereas the placebo treatment and active treatment at T28 showed an improvement in <50% of subjects.

4. Self-Assessment Questionnaire

Pleasantness of the two treatments led to positive responses at both T28 (96.8%) and at T56 (93.5%). Regarding the perception of performance, in terms of the overall appearance of facial and body skin, the active treatment obtained positive answers (score >60%) for all twenty-one items investigated at T56, and in eighteen out of twenty-one responses at T28. For the placebo group, instead, only fourteen out of twenty-one items registered a positive score >60% at T28 and T56. By the end of the treatment volunteers from the active treatment were almost unanimous (>93%) in their positive perception of facial moisturization and nourishment; the improvement in the appearance of the body was also well perceived.

5. Discussion

Skin, especially facial skin, represents one of the most important factors for attractiveness; however, at the same time, it is the part of the body that more than others is subjected to external damage which, often, causes anti-aesthetic imperfections on it [33]. These can result in alterations of skin homogeneity and appearance, and sometimes can turn into serious complications which alter the skin structural and functional integrity [4,34].

In this context, the so-called “beauty supplements” represent a valid ally to the cosmetic approach to maintain and to restore the normal aspect of the skin [5,35]. There is, in fact, strong evidence of the existing link between nutrition and skin condition which demonstrates the impact of diet, intended also as supplementation, on skin health and beauty. The beneficial role of adequate nutritional supplementation has been largely demonstrated, for example, in preventing the harmful effects of UV exposure and in managing skin aging and reactive skin [33].

As several biochemical processes are involved in the development of skin imperfections, a more comprehensive approach based on food supplements containing different typologies of ingredients, each of them with specific biological peculiarities, looks promising in managing such discomfort and achieving consistent results.

The present clinical study has shown that the oral supplementation with SelectSIEVE® Rainbow is effective, compared to the placebo, in improving female facial skin imperfections. These findings, obtained by the combined botanical extracts, correlate with the biological activity demonstrated *in vitro* [20]. In turn, the results obtained *in vitro* may be related to the biological activity of the individual components of the mixture: black rice extract, orange extract, kiwi fruit fibers, and bromelain from pineapple.

SelectSIEVE® Rainbow treatment was effective in achieving a progressive improvement throughout the study of the face skin profilometry, deep skin moisturization and skin brightness of enrolled subjects. Placebo treatment also resulted in a similar progressive trend; however, the improvement was always quantitatively higher for the active food supplement group. Moreover, intergroup differences were calculated for all instrumental parameters, and they were always statistically significant in favour of the active group over placebo.

A similar trend was recorded in the evaluation of two facial skin imperfections which have a relevant impact on women self-confidence: dark circles and eye bags. SelectSIEVE® Rainbow treatment led to higher ITA° values, indicative of a lighter skin pigmentation, that increased throughout the study with a statistically significant intergroup difference compared to the placebo group. The instrumental results were confirmed by the clinical assessment of the digital pictures acquired from the 10 subjects enrolled for such evaluation: improvement of dark circles appearance was clinically significant in SelectSIEVE® Rainbow group at T56.

Regarding eye bags volume, measured by skin profilometry, a progressive and statistically significant intragroup reduction was registered in both groups; however, such decrease was higher in the SelectSIEVE® Rainbow group, although no intergroup difference was calculated. As for the dark circles, digital pictures from the 10 enrolled subjects demonstrated a clinical improvement of the eye bags appearance only in the subjects receiving SelectSIEVE® Rainbow at T56.

Moreover, facial skin pinkish, assessed by VAS, showed a progressive and statistically significant improvement throughout the study in the active food supplement group, whereas placebo treatment resulted in a statistically significant reduction only at T56. Overall, skin pinkish was lower in the SelectSIEVE® Rainbow group and registered a clinically relevant improvement at T56, indicative of a better skin tone and complexion.

Lastly, a clinical improvement of the skin evenness complexion was appreciated in digital pictures acquired at T56 in the SelectSIEVE® Rainbow treatment.

In general, the results of the self-assessment questionnaires showed a more positive perception of the performance of SelectSIEVE® Rainbow treatment compared to the placebo treatment. Since the present study mainly focused on evaluating

the appearance of facial skin, the treated group expressed very positive answers to the related questions, concerning moisturization and nourishment; however, positive responses were also recorded for the performance of the tested product in improving the appearance of the body, in agreement with the results of the previous study.

6. Conclusion

SelectSIEVE® Rainbow oral supplementation represents a useful approach to address the multifactorial discomfort that is generically identified as skin imperfection. The mixture was developed by using botanical ingredients, well-known for their biological activities, which underwent an *in vitro* characterization, firstly individually and then as a botanical complex (data not shown). They showed antioxidant, proteolytic and hypolipidemic properties: this biological profile allows the ingredient to be used as an aid in the management of skin blemishes and cellulite.

The positive results achieved by the previous clinical study and corroborated by the current ones confirm the efficacy of SelectSIEVE® Rainbow not only against body skin imperfections, such as cellulite, but also for improving the appearance of facial skin, leading to a reduction of dark circles and under eye bags.

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8. Disclosure

The author reports no conflicts of interest in this work.

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