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Evaluation of Safety and Efficacy of Chemical Peels With and Without Sonophoresis on Selected Skin Parameters—A Prospective Comparative Study

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Abstract: Background: Skin is the largest organ in the human body. Some skin parameters like moisturization and sebum secretion play a vital role in the skin's functioning. This study aims to assess the effects of topical chemical peels of different concentrations and pH, applied manually and with ultrasounds, on the level of hydration, erythema, pigmentation, and sebum secretion of the skin. Methods: The study involved 90 Caucasian females, aged 25 to 59, with dry, dehydrated skin, skin with erythema or pigmentation disorders. The patients were randomly divided into three equal groups. The subjects from Group A were applied 10% mandelic acid with 25% gluconolactone of pH 4.0 manually. In Group B, 40% mandelic acid of pH 1.5 was used. The subjects from Group C were applied 10% mandelic acid with 25% gluconolactone of pH 4.0 via sonophoresis. A series of six procedures in weekly intervals was performed. Skin functional parameters (skin hydration, erythema, and melanin indicators) were taken before the first procedure, after 14 days, 28 days, and 42 days. Results: In Group A, the level of moisturization of the skin increased statistically significantly (p = 0.0100) however, the sebum secretion and erythema did not change. In Group B, the level of moisturization improved statistically significantly, as well as erythema (p = 0.0001). Sebum secretion in the final measurement increased. The moisturization and erythema in Group C did not differ statistically significantly. On the other hand, the sebum secretion increased significantly. Conclusions: Very superficial chemical peels significantly alter selected skin parameters. AHAs and PHAs applied using the ultrasound method do not affect the level of hydration, erythema, or pigmentation of the skin.

Keywords: dermatology; chemical peels; mandelic acid

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1. Introduction

1.1. Skin, Its Functions and Disorders

Skin is the largest organ in the human body and covers an area of approximately 2 m^2 [1]. It serves as a protective barrier against the external environment and is the first line of defense against physical, mechanical, chemical, and bacterial factors. In addition, it functions as a sensory organ, shields the internal organs, and maintains proper moisture levels. The skin is made up of three main layers: epidermis, dermis, and hypodermis (also known as the subcutaneous tissue).

Some skin parameters like moisturization and sebum secretion play a vital role in the skin's functioning and its barrier properties. Research shows that dry, dehydrated skin is a great discomfort for patients, and up to 30% of them worldwide are affected by this phenomenon [2]. Water is the factor that provides proper skin functioning. Deprivation of the proper amount of water results in faulty skin functioning, itchiness, roughness, excessive keratinization, and skin irritation. Heretofore, the therapies aimed at increasing skin hydration were based mainly on repairing the epithelial skin barrier. Nowadays, it is

known that rehydration of the skin is a multifaceted process, thoroughly related to peeling and exfoliation.

Pigmentation disorders have always been a challenging dermatological issue. Hyperpigmentation changes are caused by the disturbance in the synthesis and arrangement of the natural skin pigment, i.e., the melanin. Melanin is produced in the melanocytes which are found in the stratum basale, the deepest layer of the five layers of the epidermis. Types of hyperpigmentation include melasma, freckles, lentigo, or post-inflammatory discoloration. Despite numerous topical preparations applied on the skin, reducing hyperpigmentation can pose a significant challenge in everyday practice.

Another great aesthetic and dermatological issue manifested by increased vascular activity is known as erythema and telangiectasia. Telangiectasias are localized in the papillary dermis and are visible through the epidermis as a single or a group of dilated vessels. Constant exposure to external environmental factors such as UV radiation, wind, temperature differences, inadequate skincare, certain medications, stress, caffeine, or nicotine makes the skin of the face predisposed to the development of pathological conditions like increased vascular activity, dryness, and also pigmentation disorders. Despite many methods and formulations available, the choice of a proper procedure to effectively increase the skin moisturization level, improve its pigmentation, and resolve the dry skin with erythema can pose a challenge.

1.2. Chemical Peels

Exfoliation with chemical peels has been widely known and used in dermatology for decades. The first to discover the exfoliating properties of chemicals were ancient Egyptians in 1550 BC [3]. For peeling procedures, alpha-hydroxy acids (AHAs) contained in sour milk were used. Egyptian women wiped their faces with slices of citrus fruits and wine residue to remove the outer layer of the epidermis. As a result, their skin became not only brighter but also smoother and softer. What is more, the Romans and Greeks used compresses containing highly irritating substances to improve the appearance of their skin. Popular exfoliants were also pumice, myrrh, and resins, which were added to chemical peels. Ferdinand von Hebra, a dermatologist from Vienna, is credited with bringing peels to the attention of medical professionals. He attempted to remove freckles and pigmentation in 1884 by employing solutions of sulfuric, acetic, and hydrochloric acids. Nonetheless, significant skin damage resulted from the extended application duration and the use of powerful irritants.

Preparations belonging to the group of chemical peels are agents that, when applied topically to the skin, cause controlled damage to the epidermis or dermis. This leads to the activation of a cascade of repair reactions that affect the replacement of part or all of the epidermis. It can also initiate the process of collagen remodeling. Chemical peels can be divided into several basic groups depending on the depth of penetration as shown in Figure 1. Examples of certain peels according to their penetration are presented in Figure 2.

1.2.1. Characterization of Alpha-Hydroxy Acids (AHAs)

Alpha-hydroxy acids (α-hydroxy acids; AHAs), called fruit acids, belong to the group of very superficial chemical peels [4]. They are obtained from sugar cane, willow bark, milk, fruit, almonds, and are commonly found in nature. They can also be obtained by chemical synthesis [5]. The AHA group consists of the following acids: glycolic, lactic, malic, tartaric, citric, and mandelic acid [6].

Mandelic acid (2-hydroxyphenylacetic acid) is a product of natural origin [7], obtained by hydrolysis of bitter almond extract (*Amygdalus communis* var. *amara*), apricot, and cherry [8]. The mandelic acid molecule is quite large, it is made up of eight carbon atoms, which is why it penetrates more uniformly and gently than other acids, including glycolic acid [9]. Mandelic acid is devoid of irritating effects, therefore it can be used in patients with sensitive, thin, dry, and dehydrated skin. Furthermore, it is characterized by bactericidal, bacteriostatic, and depigmenting properties, and does not have a photosensitizing

effect [10]. Low concentration mandelic acid, such as 10%, acts mainly on the skin surface and provides a gentle exfoliation of the epidermis. It proves to be effective at evening out the skin tone, reducing minor discolorations, and improving skin hydration. A higher concentration of mandelic acid (40%) allows a deeper exfoliation of the epidermis. It might be intended for people with oily and acne-prone skin, with more visible discolorations and acne scars.

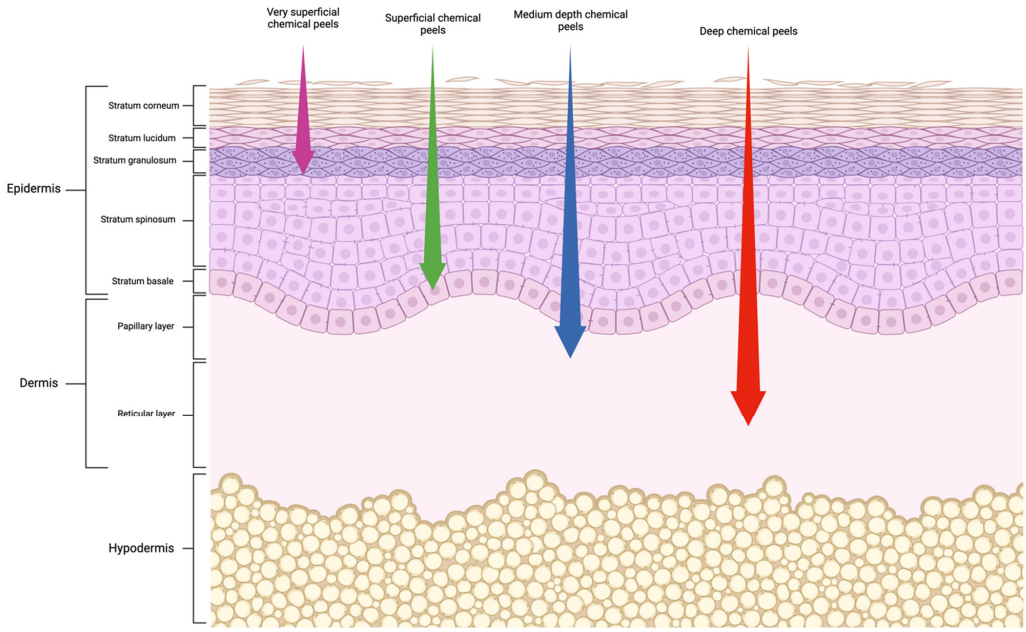

Figure 1. Depth penetration of chemicals peels (based on own PhD dissertation).

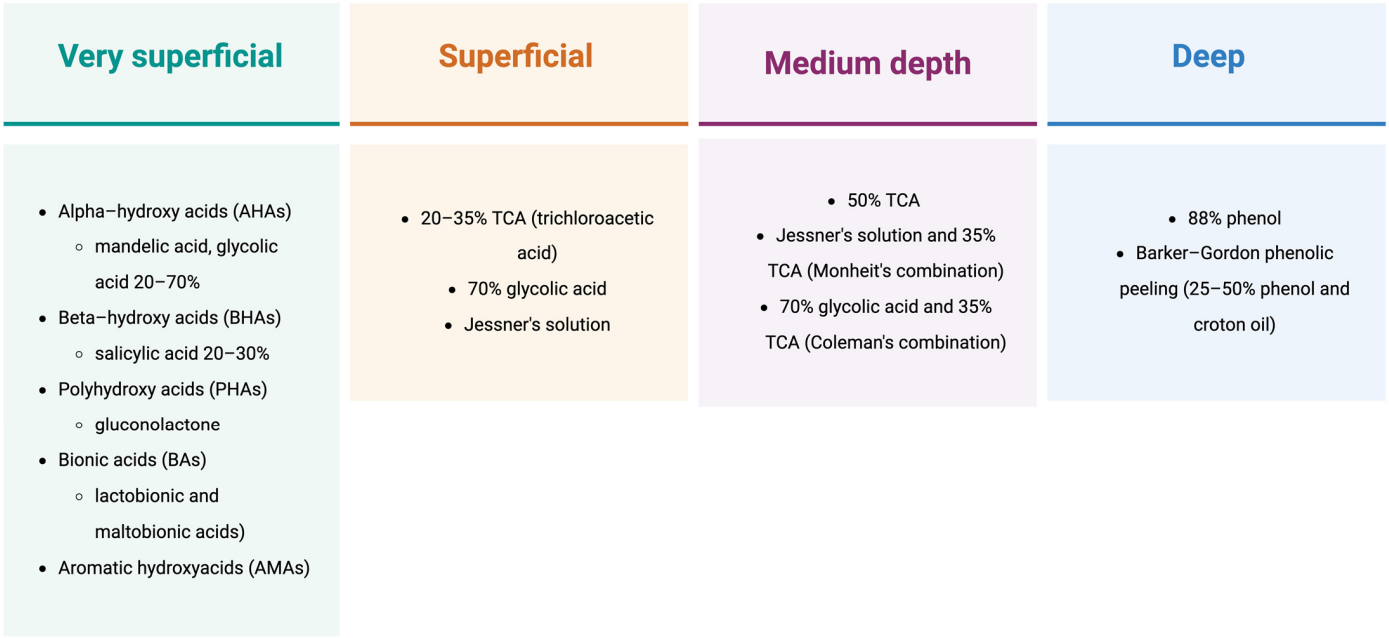

Figure 2. Groups of chemical peels depending on the depth of penetration. (based on own PhD dissertation).

1.2.2. Characterization of Polyhydroxy Acids

Gluconolactone belongs to the group of polyhydroxy acids. Its action is similar to that of AHA; however, it is said to have a reduced irritant potential. It is characterized by antioxidant properties, comparable to ascorbic acid and alpha-tocopherol [11]. Moreover, it

is effective in improving moisturization and evening out skin tone [12]. It can be applied for dry, sensitive, dehydrated skin, as well as in atopic skin [13]. Gluconolactone is often used in combination with other AHAs, including mandelic acid. The concentration of gluconolactone directly affects the intensity of the exfoliation effect. The higher the concentration, the deeper and more effective the exfoliation. Higher concentrations also increase its regenerative and anti-aging properties. The pH of gluconolactone determines how deeply it penetrates the skin. A lower pH enhances the exfoliating effect, but at the same time increases the risk of irritation. Both parameters should be adapted to the individual needs of the patient and their skin type to optimize therapeutic effects while minimizing the risk of side effects.

Our study aimed to assess the impact of superficial chemical peels as well as to compare the effects of topical chemical peels of different concentrations and pH, applied manually and with ultrasounds, on the level of hydration, erythema, pigmentation, and sebum secretion of the skin. Moreover, it aimed to indicate the most effective treatment procedure, concentration, and pH of the compared topical chemical peel.

2. Materials and Methods

This prospective, comparative study comprised 90 Caucasian women (age range from 25 to 59; mean age 38 years) with dry, dehydrated skin with erythema, and pigmentation disorders (Fitzpatrick II–III skin phototypes).

The inclusion criteria were the following:

- Female patient over the age of 18 years;
- Skin condition: dry, dehydrated skin, with erythema or pigmentation disorders (i.e., melasma, freckles, post-inflammatory hyperpigmentation).

The exclusion criteria were the following:

- Pregnancy or breastfeeding;
- Disrupted epithelial continuity;
- Hypersensitivity to any of the ingredients used in the formulations;
- Both acute and chronic infections and contagious diseases: tuberculosis and herpes simplex;
- Taking isotretinoin within the past 6 months;
- Epilepsy;
- Emotional instability;
- Surgical procedures in the facial region within the past 6 months;
- Tendency to form keloids;
- Skin conditions: rosacea, atopic skin inflammation, contact dermatitis, sebaceous dermatitis;
- Having any electronic devices in the body (i.e., pacemaker).

The recruitment process and assessment were performed by two investigators (a dermatologist with over 20 years of experience and a specialist in cosmetology with over 15 years of experience).

An informed written consent was signed by all patients. Moreover, each participant completed a questionnaire before (questionnaire 1) and after (questionnaire 2) the completion of the study. The study protocol has been approved by the Bioethical Committee at the Medical University of Gdańsk, registry number NKBBN187/2014.

The patients were randomly divided into three groups, with 30 subjects in each. The subjects from group 1 (Group A) were applied 10% mandelic acid with 25% gluconolactone of pH 4.0 manually. The subjects from group 2 (Group B) were manually applied 40% mandelic acid of pH 1.5. The subjects from Group 3 (Group C) were applied 10% mandelic acid with 25% gluconolactone of pH 4.0 via ultrasounds (sonophoresis). The apparatus emitting ultrasounds of 1 MHz was used. The subjects received a series of six procedures, carried out at weekly intervals. The amount of product used was 3 mL per subject (face only, leaving 5 mm of lid margin to prevent solution from entering into the eyes). Prior to the

procedure, the skin was disinfected and dried. A thin layer of petroleum jelly was applied to sensitive areas such as nasolabial folds and lateral canthi. Eye protection with shields was provided to cover the eyes. Each treatment session in each subject was performed by the same practitioner (specialist in cosmetology with over 15 years of experience). Skin functional parameters were taken before the first procedure (Measurement 1), after 14 days (Measurement 2), 28 days (Measurement 3), and after 42 days (Measurement 4).

All the measurements were aimed to assess the degree of achieved epithelial moisturization. The degree of epithelial moisturization was evaluated by using Corneometer® MC900–Courage + Khazaka Electronic GmbH (Köln, Germany). The method of measuring the hydration of the stratum corneum (SC) is a capacitive method and allows to assess the electrical capacity of the upper layers of the epidermis to a depth of approximately 10–20 μm. When the epidermis is dehydrated, due to the dielectric constant of water, the electrical capacity of the SC changes proportionally. The higher the value of the corneometric measurement, the better the degree of hydration of the epidermis. Erythema and melanin were evaluated utilizing Mexameter® MC900–Courage + Khazaka Electronic GmbH (Köln, Germany). The erythema index was measured with light with a wavelength of 568.560 nm, while melanin was measured with light with a wavelength of 880 nm. The measurements were made by perpendicular application of the probes to the surface of the skin. The measurements were carried out in the same conditions—in the same room with a temperature of 20–22 °C and relative air humidity of 50–60%. The patients acclimatized for 30 min. The same measurement time was maintained for each patient.

Statistical Analysis

All statistical calculations were carried out using the StatSoft statistical package. Inc. (Tulsa, OK, USA) (2011). STATISTICA (data analysis software system) version 10.0. www.statsoft.com and an Excel spreadsheet.

Quantitative variables were characterized by arithmetic mean, standard deviation, median, minimum and maximum values (range), and 95% CI (confidence interval). On the other hand, categorical variables are presented by counts and percentages (percentages).

To check whether the quantitative variable came from a population with a normal distribution, the Shapiro–Wilk W test was used. On the other hand, the Leven (Brown–Forsythe) test was used to test the equal-variance hypothesis.

The significance of the differences between the two groups (unrelated variables model) was examined by tests of the significance of differences: the Student's *t*-test (or in the absence of homogeneity of variance, the Welch test) or the Mann–Whitney U-test (in the case of failure to meet the conditions for the applicability of the Student's *t*-test or for variables measured on an ordinal scale). The significance of differences between more than two groups was checked by the F (ANOVA) or Kruskal–Wallis test (in case of failure to meet the conditions for ANOVA applicability). In the case of statistically significant differences between the groups, post hoc tests were used (Tukey's test for F, Dunn's test for Kruskal–Wallis).

In the case of the model of two related variables, the Student's *t*-test or the Wilcoxon pair order test was used (in the case of failure to meet the conditions for the applicability of the Student's *t*-test or for variables measured on an ordinal scale). The significance of differences between more than two related variables in the model was checked by the analysis of variance with repeated measures or the Friedman test (in the case of failure to meet the conditions for the applicability of the analysis of variance with repeated measures or for variables measured on an ordinal scale).

Chi-square tests of independence were used for qualitative variables (using Yates correction for cell counts below 10, checking Cochran conditions, and Fisher's exact test, respectively).

In order to determine the relationship between the strength and direction between the variables, a correlation analysis was used by calculating the Pearson and/or Spearman

correlation coefficients. All calculations were based on the significance *p*-value equal to 0.05.

3. Results

During the investigation period, a total of 90 participants agreed to take part and finished the study. The results are shown on Figures 3–6.

Figure 3. The patient (**A**) before the application of 10% mandelic acid and 25% gluconolactone with pH 4.0 applied manually (**B**) after the application of a series of six treatments of 10% mandelic acid and 25% gluconolactone with pH 4.0, applied manually.

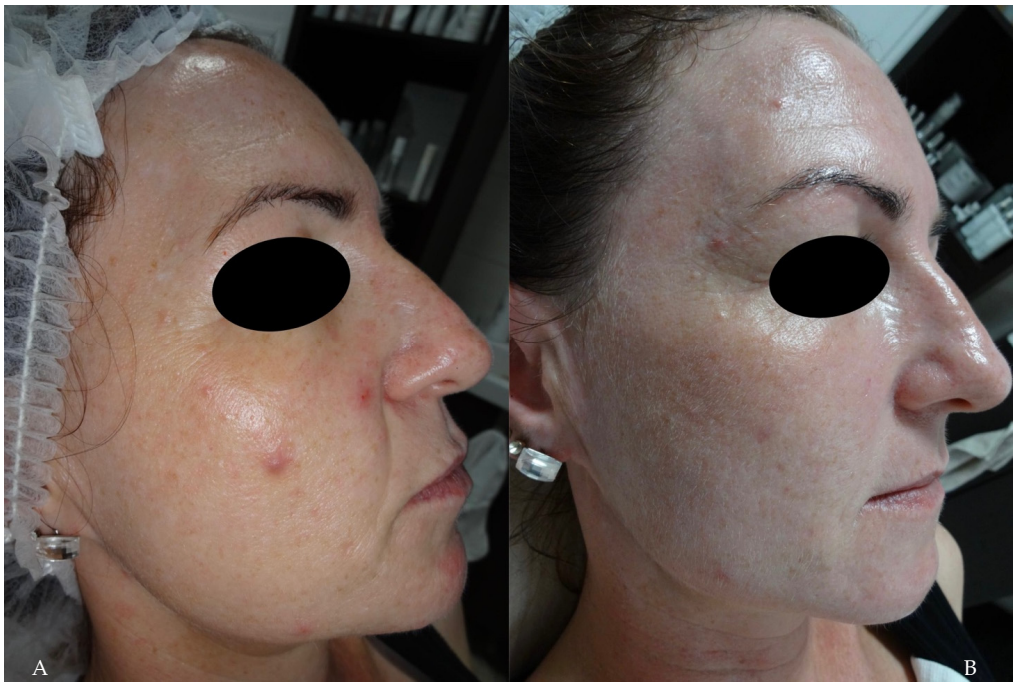

Figure 4. The patient (**A**) before the application of 40% mandelic acid with pH 1.5 applied manually, and (**B**) after a series of six treatments with 40% mandelic acid with pH 1.5 applied manually.

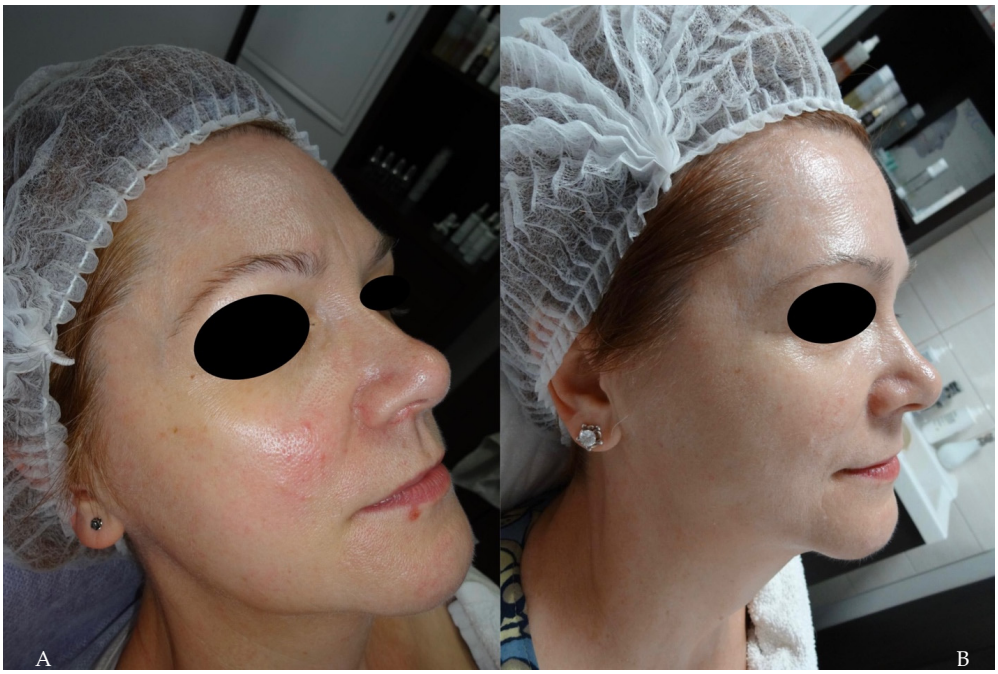

Figure 5. The patient (**A**) before the application of 40% mandelic acid with pH 1.5 manually, and (**B**) after the application of a series of six treatments with 40% mandelic acid with pH 1.5.

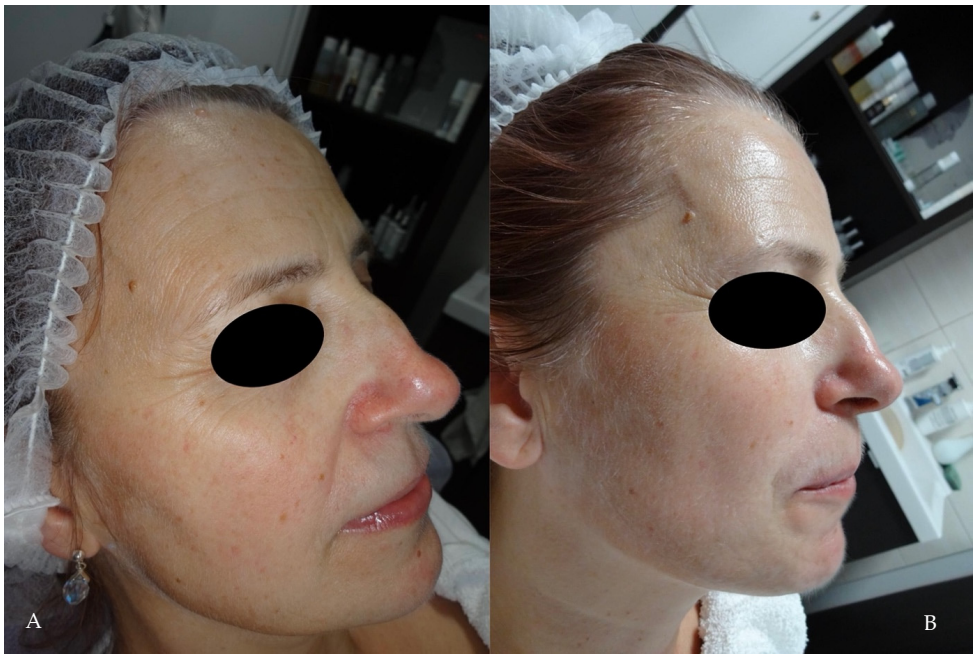

Figure 6. The patient (**A**) before the application of 10% mandelic acid and 25% gluconolactone with pH 4.0 applied manually, and (**B**) after the application of a series of six treatments with 10% mandelic acid and 25% gluconolactone with pH 4.0 applied manually.

3.1. Skin Moisturization

The mean hydration in Measurement 1 for Group A was 52.5 (7.0) (range 40.5–65.8), for Group B it was 52.2 (7.3) (range 35.3–66.3), and for Group C it was 55.8 (6.7) (range 39.3–69.5). In the baseline measurement, no statistically significant differences in hydration were found due to the groups under consideration (p = 0.1266).

The mean hydration in measure 4 for Group A was 71.6 (5.4) (range 61.4–83.8), for Group B it was 62.7 (5.0) (range 52.3–71.4), and for Group C it was 66.8 (5.2) (range 54.1–77.0).

After the fourth measurement, hydration differed statistically significantly in the study groups (p = 0.0001). Patients from Group A were characterized by significantly higher hydration compared to Group B (p = 0.0001) and Group C (p = 0.0028). Moreover, Group B had significantly higher hydration compared to the Group C (p = 0.0113). After the final measurement, the probands from Group A were characterized by the highest hydration. Detailed data are provided in Table 1.

Table 1. Group characteristics according to skin moisturization.

	Group A (n = 30)	**Group B (n = 30)**	**Group C (n = 30)**	***p*-Value**
Measurement 1				0.1266
Mean (SD)	52.5 (7.0)	52.2 (7.3)	55.8 (6.7)	
Range (min.–max.)	40.5–65.8	35.3–66.3	39.3–69.5	
Median	52.0	52.0	57.5	
Measurement 2				0.0001
Mean (SD)	62.8 (7.4)	56.3 (5.8)	65.8 (5.0)	0.0020
Range (min.–max.)	46.4–73.5	45.4–67.9	54.9–75.5	0.0005
Median	63.7	56.9	65.6	
Measurement 3				0.0001
Mean (SD)	70.9 (6.6)	57.9 (5.7)	60.5 (7.2)	0.0001
Range (min.–max.)	59.4–85.5	44.8–67.8	49.9–73.3	0.0002
Median	70.9	57.1	62.6	
Measurement 4				0.0001
Mean (SD)	71.6 (5.4)	62.7 (5.0)	66.8 (5.2)	0.0001
Range (min.–max.)	61.4–83.8	52.3–71.4	54.1–77.0	0.0028
Median	72.6	63.4	68.3	0.0113

In Group A, the level of moisturization of the skin changed statistically significantly (p = 0.0100). The moisturization in measurements 2, 3, and 4 increased statistically significantly, compared to the initial measurement (p = 0.0001). Moisturization in the final measurement did not alter statistically significantly, compared to the moisturization level as assessed in measurement 3 (p = 0.8375).

In Group B, during the time of procedures, the moisturization altered significantly statistically (p = 0.0001). Moisturization in measurements 2, 3, and 4 increased significantly statistically, comparing to the initial measurement outcome (measurement 1 vs. measurement 2, p = 0.0009; measurement 1 vs. measurement 3, p = 0.0002; measurement 1 vs. measurement 4, p = 0.0002). Moreover, the moisturization in measurement 4 increased significantly, compared to the initial measurement result (p = 0.0002). The moisturization in the final measurement increased compared to the moisturization level in measurement 3 (p = 0.0069). The moisturization in measurement 3 did not differ statistically significantly in comparison to the final measurement (p = 0.5185).

The moisturization in Group C tested during the procedures did not differ statistically significantly (p = 0.6433). The greatest improvement in moisturization in all three groups occurred on average after the third measurement.

3.2. Sebum Secretion

The mean sebum secretion in measurement 1 for Group A was 23.6 (19.5) (range 4.5–82.0), for Group B it was 22.4 (11.8) (range 3.5–46.0), and for Group C it was 24.1 (12.3) (range 5.0–51.0). No statistically significant differences in sebum secretion were found in the baseline measurement compared to the studied groups (p = 0.6132).

The mean sebum secretion in measurement 4 for Group A was 34.2 (13.6) (range 17.5–71.5), for Group B it was 28.8 (9.2) (range 15.8–50.5), and for Group C it was 35.9 (10.6) (range 19.0–58.3). No statistically significant differences in sebum secretion were found in the final measurement compared to the studied groups ($p = 0.0771$). Detailed data are provided in Table 2.

Table 2. Group characteristics according to sebum secretion.

	Group A (*n* = 30)	**Group B (*n* = 30)**	**Group C (*n* = 30)**	***p*-Value**
Measurement 1				0.6132
Mean (SD)	23.6 (19.5)	22.4 (11.8)	24.1 (12.3)	
Range (min.–max.)	4.5–82.0	3.5–46.0	5.0–51.0	
Median	13.8	21.8	25.0	
Measurement 2				0.4805
Mean (SD)	21.4 (13.1)	23.6 (10.3)	26.5 (12.5)	
Range (min.–max.)	4.0–43.0	4.0–48.5	1.0–46.3	
Median	22.0	23.5	27.5	
Measurement 3				0.1212
Mean (SD)	25.2 (16.6)	26.6 (14.9)	30.9 (8.9)	
Range (min.–max.)	2.3–64.8	7.8–60.0	18.8–51.0	
Median	20.8	23.0	27.8	
Measurement 4				0.0771
Mean (SD)	34.2 (13.6)	28.8 (9.2)	35.9 (10.6)	
Range (min.–max.)	17.5–71.5	15.8–50.5	19.0–58.3	
Median	35.0	27.5	36.8	

As regards the sebum secretion, in Group A it did not vary statistically significantly ($p = 0.2218$).

In Group B, the sebum secretion differed statistically significantly ($p = 0.0226$) between procedures. Sebum secretion in the final measurement increased, compared to the sebum secretion measured during the final test ($p = 0.0387$). All other results did not show a statistically significant difference ($p > 0.05$).

Secretion of the sebum in Group C tested during the procedures did differ statistically significantly ($p = 0.0001$). The secretion of the sebum in measurements 3 and 4 increased statistically significantly compared to the initial sebum secretion level observed: (measurement 1 vs. measurement 3, $p = 0.0153$; measurement 1 vs. measurement 4, $p = 0.0002$). Moreover, the sebum secretion in measurement 4 increased statistically significantly compared to the initial sebum secretion level ($p = 0.0009$). Sebum secretion in the final measurement did not differ significantly in comparison to the sebum level measured in the initial test ($p = 0.1668$). Sebum secretion in the initial measurement differed significantly, as compared to measurement 2 ($p = 0.6461$) and measurement 3 ($p = 0.2387$). The greatest improvement in sebum secretion in the three groups occurred on average after two measurements (the median measurement for all was 2).

3.3. Erythema

Mean erythema and redness in measurement 1 for Group A was 33.6 (7.3) (range 20.8–55.0), for Group B it was 34.3 (6.3) (range 24.0–54.8), and for Group C it was 34.0 (6.0) (range 22.0–48.3). No statistically significant differences in redness were found in the baseline measurement compared to the study groups ($p = 0.9120$).

The mean erythema and redness in measurement 4 for Group A was 33.2 (6.0) (range 21.0–43.5), for Group B it was 30.3 (4.3) (range 23.4–43.3), and for Group C it was 29.7 (4.4)

(range 21.9–43.6). Erythema and redness were significantly higher in Group A compared to Group C ($p = 0.0298$). Detailed data are provided in Table 3.

Table 3. Group characteristics according to erythema.

	Group A ($n = 30$)	Group B ($n = 30$)	Group C ($n = 30$)	p-Value
Measurement 1				0.9120
Mean (SD)	33.6 (7.3)	34.3 (6.3)	34.0 (6.7)	
Range (min.–max.)	20.8–55.0	24.0–54.9	22.0–48.3	
Median	33.5	34.0	34.3	
Measurement 2				0.7132
Mean (SD)	34.2 (7.2)	32.9 (4.7)	32.9 (4.1)	
Range (min.–max.)	22.1–52.9	25.4–40.5	26.3–38.9	
Median	33.8	33.6	33.4	
Measurement 3				0.2268
Mean (SD)	34.6 (6.1)	31.8 (5.0)	32.6 (7.4)	
Range (min.–max.)	20.8–46.5	23.9–45.1	22.6–50.1	
Median	34.5	32.6	33.1	
Measurement 4				0.0216
Mean (SD)	33.2 (6.0)	30.3 (4.3)	28.7 (4.4)	0.0298
Range (min.–max.)	21.0–43.5	23.4–43.3	21.9–43.6	
Median	34.8	29.6	29.9	

In the Group A, the tests performed during the procedures showed that erythema or facial redness did not change statistically significantly ($p = 0.0507$).

In the Group B, erythema and facial redness differed significantly ($p = 0.0001$). Both erythema and facial redness decreased in the final measurement, comparing to the values obtained in the initial tests ($p < 0.05$). Moreover, both parameters in the final measurement decreased in comparison to the measurement 2 ($p < 0.05$). In all other measurement results, no statistically significant differences were detected ($p > 0.05$).

Erythema and facial redness in Group C, tested during the procedures, did not show statistically significant differences ($p = 0.7380$). There was a statistically significant difference compared to the study groups ($p = 0.0025$) in terms of erythema improvement. In Group A, the improvement in erythema occurred significantly faster (in the third measurement) compared to the 40% and Group C, where the improvement occurred after the fourth measurement ($p < 0.05$).

3.4. Pigmentation

The mean pigmentation in measurement 1 for Group A was 12.6 (3.8) (range 6.3–20.3), for Group B it was 12.3 (3.2) (range 5.3–18.5), and for Group C it was 13.1 (5.0) (range 4.5–28.8). No statistically significant differences in pigmentation were found in the baseline measurement compared to the study groups ($p = 0.7317$).

The mean pigmentation in measure 4 for Group A was 12.2 (4.1) (range 7.3–24.1), for Group B it was 11.8 (3.0) (range 6.5–20.3), and for Group C it was 11.1 (3.3) (range 2.8–20.0). No statistically significant differences in pigmentation were found in the final measurement compared to the study groups ($p = 0.7777$). Detailed data are provided in Table 4.

In Group A, no statistically significant pigmentation difference occurred ($p = 0.8232$). Moreover, in Group B, the pigmentation did not differ statistically significantly, either ($p = 0.6833$). In Group C, pigmentation did not differ statistically significantly during the procedure, either ($p = 0.9390$).

In Group A, together with the increase of moisturization, sebum secretion was decreasing in the measurement 2 (correlation coefficient: -0.60, $p = 0.0180$), in the measurement 3 (correlation coefficient: -0.56, $p = 0.0020$) as well as in the measurement 4 (correlation coefficient -0.50, $p = 0.0090$).

Table 4. Group characteristics according to pigmentation.

	Group A (*n* = 30)	**Group B (*n* = 30)**	**Group C (*n* = 30)**	***p*-Value**
Measurement 1				0.7317
Mean (SD)	12.6 (3.8)	12.3 (3.2)	13.1 (5.0)	
Range (min.–max.)	6.3–20.3	5.3–18.5	4.5–28.8	
Median	12.0	12.5	12.1	
Measurement 2				0.7744
Mean (SD)	12.3 (2.7)	11.9 (2.1)	12.3 (3.5)	
Range (min.–max.)	7.9–17.9	7.6–16.3	5.9–18.9	
Median	11.6	12.1	12.0	
Measurement 3				0.7935
Mean (SD)	12.1 (3.6)	11.8 (3.0)	11.9 (3.2)	
Range (min.–max.)	7.6–23.6	6.5–19.5	4.5–17.5	
Median	11.1	11.0	12.4	
Measurement 4				0.7777
Mean (SD)	12.2 (4.1)	11.8 (3.0)	11.1 (3.3)	
Range (min.–max.)	7.3–24.1	6.5–20.3	2.8–20.0	
Median	11.0	11.8	11.3	

In Group B, with the increase in moisturization, sebum secretion decreased in measurement 4 (correlation coefficient -0.48, $p = 0.0200$). For all dependencies, no statistically significant correlations were determined.

No statistically significant correlations were found between the age of the subject who was undergoing the procedures, and the best results obtained. Therefore, the study inclusion criterion which involved the age of the subjects was found to be irrelevant.

3.5. Questionnaires After the Completion of the Study

The questionnaires included questions about improvement after the completion of the study in the scope of a reduction of skin itching, reduction of skin stinging, reduction of skin tightness, reduction of skin burning, reduction of skin redness, reduction of skin peeling, reduction of pain, and reduction of skin roughness. The respondents were asked to answer 'yes', 'no', or 'insignificantly'. Moreover, we asked after which treatment the patients noticed the greatest improvement.

Statistical analysis of the questionnaire completed by the subjects showed that all the examined patients subjectively stated that the greatest, satisfactory improvement in skin parameters occurred after the second treatment.

The main parameters that improved in the subjective assessment of the respondents were: improvement in smoothness, observed in all groups (96.7% of the respondents), reduction of skin roughness observed in the following groups: Group A—83.3%, Group B—70%, and Group C—80%. Reduction of unpleasant skin tightness observed in the group: Group A—83.3%, Group B—70%, Group C—76.7% of the subjects, as well as reduction of skin redness observed in the group: Group A—63.3%, Group B—46.7%, and Group C—60% of the patients.

4. Discussion

In the present study, we assessed the efficacy and safety of topical chemical peels of different concentrations and pH, applied manually and with ultrasounds, on the level of hydration, erythema, pigmentation, and sebum secretion of the skin. Dry, dehydrated skin is characterized by an excessive amount of corneocytes on the surface of the stratum

corneum. The increased number of cells of the stratum corneum is a consequence of a disturbance in the exfoliation process. The first reaction of dehydrated skin to the application of acid is thinning manifested by reducing the thickness of the stratum corneum. However, it is believed that with repeated use of AHAs, the thickness of the epidermis returns to its normal size. After a series of treatments, the stratum corneum becomes thicker, tighter, and compact, and as a result, it becomes more resistant to excessive water loss [14]. Proksch and Lachapelle also report that the application of AHA in a series initially results in a reduction of the stratum corneum, and consequently, it is remodeled and returned to the appropriate thickness [15].

Our study also confirms the above-mentioned. As a result of the application of 10% mandelic acid, 25% gluconolactone, and 40% mandelic acid applied manually, there was a significant increase in hydration. Most likely, one of the processes leading to the observed increase in skin hydration was based on the mechanism of exfoliation and thickening of the stratum corneum.

Literature data report that higher concentrations of very superficial chemical peels induce corneodesmolysis, while lower concentrations have a milder effect on reducing the cohesion of corneocytes [16]. A less aggressive mechanism can be more effective on dry skin with a low level of hydration. Corneodesmolysis, initiated by high-concentration, low-pH peels, occurs through a released proton that comes from the acid. It induces the hydrolysis of peptide bonds found in desmosomes [17].

In their experiments, Berardesca et al. applied low concentrations of chemical peels—three types of 8% AHA: glycolic acid (GA, pH 4.4), lactic acid (LA pH 4.4), tartaric acid (TA 3.4), and PHA—gluconolactone (GLU, pH 4.3) [18]. Their results indicate that AHAs and PHAs, despite their low concentrations, had a significant effect on SC, consisting in improving the functioning of the skin barrier. Researchers suggest that the improvement of the corneal barrier is influenced by the reduction of corneocyte cohesion by modification of ionic bonds and enzymatic inhibition of sulfonotransferases, phosphotransferases, and kinases formed as a result of the action of AHAs and PHAs with low concentration and high pH.

In our research, the highest, significant increase in the level of hydration was recorded in Group A. A lesser, but also significant, increase in the degree of skin hydration was obtained in Group B. The results obtained can be rationalized by two factors, the skin type and the addition of 25% gluconolactone to the peel used in Group A. Dry skin is vastly prone to irritation. AHAs and PHAs with low concentrations and high pH have a milder effect on reducing the degree of corneocyte adhesion, with a reduced irritant potential. The effect of reducing the adhesion of stratum corneum (SC) cells is their separation and exfoliation, and consequently, an increase in the degree of hydration of the epidermis. Furthermore, the gluconolactone, which is characterized by the ability to absorb water and strengthen the epidermal barrier, used in our study could additionally increase the level of skin hydration. This preparation gradually penetrates the skin without causing irritation.

The introduction of active substances with the use of ultrasound (sonophoresis) results in an increase in the permeability of SC [19]. This process is based on the mechanism of local change in the permeability of the stratum corneum as a result of cavitation. The actual action of cavitation is mainly induced in the coupling medium [20]. As a result of interaction with ultrasound, cavitation bubbles come into contact with the skin, under the influence of which the lipid bilayer structures of the SC are disturbed. It leads to an increase in the local permeability of the epidermal barrier based on two mechanisms. The first one consists of disturbing the structure of lipoids—disturbing their two-layer arrangement and increasing the diffusion coefficient of solute [21]. The second mechanism is the result of a higher level of interference and is based on the loss of integrity of lipid systems, which results in an increase in the penetration of the active substance into the skin. These mechanisms only occur properly if the appropriate coupling medium is used [22].

Mandelic acid dissolves in fats, alcohol, and less so in water. The preferred substrate for it is lipophilic. In our studies, no significant increase in the level of hydration was noted

as a result of the use of 10% mandelic acid and 25% gluconolactone with a pH of 4.0. The preparations used were placed in a substrate containing a slightly oily formula. The form of the substrate was dictated by the glycerin content in the preparation. The substrate used in the preparation was a coupling substance. If too thick a coupling agent is used, i.e., paraffin oil or petroleum jelly, the penetration of the active substance into the skin may be worse [23].

Facial erythema is made up of permanent, dilated blood vessels showing through the epidermis. Rich innervation of skin vessels in the facial area affects the lively vascular play in this area of the body, stimulated by exogenous and endogenous factors [24].

The group of parameters affecting the effectiveness of AHAs includes bioavailability, pH, acid strength and concentration, type of substrate, and skin condition [25]. Van Scott and Yu report that lower concentrations and higher pH of topical AHAs produce less exfoliating effect compared to acids used at higher concentrations with a lower pH. On the other hand, the use of higher concentrations and lower pH of chemical peels leads to a significant thickening of the stratum corneum [26]. Haward et al. report that as a result of the application of alpha-hydroxy acids of different concentrations, greater epidermal thickening occurred under the influence of AHA of higher concentration [27]. In the study, acids were compared—25% glycolic acid and 12% lactic acid. The results indicate that the thickness of the stratum corneum increased by 25% as a result of the application of acid of higher concentration.

The results obtained in our research could confirm the literature data. The use of mandelic acid with a lower pH and higher concentration could have resulted in the thickening of the epidermis and reduced the visibility of skin erythema. In our study, a statistically significant reduction in erythema was obtained only in the group in which 40% mandelic acid with pH 1.5 was applied manually. Probably, the 40% mandelic acid with pH 1.5 used in our study was able to indirectly affect the deeper layers of the epidermis. Thickening of the epidermis may have reduced the visibility of translucent, dilated blood vessels through the skin, which manifested itself in a reduction in skin erythema. The lack of significant reduction in skin redness when 10% mandelic acid with pH 4.0 was applied manually and with the use of ultrasound was most likely due to too limited penetration of the acid into the skin. The shallow, very superficial effect of 10% mandelic acid on the skin did not cause a statistically significant reduction in erythema.

The mechanism of action of glycolic and lactic acid is based on the inhibition of melanin synthesis by direct inhibition of tyrosinase activity. These acids also, as a result of prolonging the transit time of cells, increase the penetration of brightening preparations. Another mechanism involves the exfoliation of melanin-containing keratinocytes, resulting in a reduction in skin hyperpigmentation [28].

Garg et al. [29]. in their experiments divided patients with acne and hyperpigmentation into two groups. The first group was given 35% glycolic acid, while the second group was given a mixture of 20% salicylic acid and 10% mandelic acid. A significant decrease in hyperpigmentation was noted in both groups. Despite the fact of visual differences in pigmentation, which were noted by the authors of the study, greater evenness of skin tone occurred in the group where salicylic and mandelic acids were applied. No statistically significant differences were found in terms of pigmentation between the two groups.

Our results indicate that no statistically significant changes in pigmentation were found in all the study groups. The brightening effect of mandelic acid is based on the exfoliation of melanin-containing cells. As a result of the reduction of cohesion between corneocytes, the process of exfoliation occurs, which in turn can lead to an even skin tone.

Mandelic acid is characterized by the presence of an aromatic ring, which determines its lipophilic properties and allows it to penetrate within the sebaceous glands. In addition, the structure of the follicle-sebaceous duct may affect the increased penetration of active substances. The stratum corneum of the duct gradually thins deep into the bellows canal and almost disappears at the point of contact with the sebaceous duct. Knaggs reports

that in these places, the SC may constitute an incomplete barrier, thanks to which the penetration of active substances into the skin is facilitated [30].

In our study, in Group A, in which mandelic acid was applied manually, no significant change in the level of sebum secretion was noted. This result may be a consequence of the significant increase in skin hydration in this group obtained in our research.

The role of ensuring the tightness of the epidermal barrier is attributed to endogenous glycerol, which is the main component of triglycerides contained in skin sebum. Fluhr et al. report that the decrease in skin hydration occurs in parallel with the decrease in endogenous glycerol levels [31]. These studies may suggest that a decrease in the level of hydration may stimulate the sebaceous glands to produce sebum, which contains triglycerides and their main ingredient—glycerol, which restores the proper level of hydration.

It is highly probable that as a result of applying a preparation on dry skin that significantly increases skin hydration and achieves homeostasis of the epidermal barrier, the level of sebum secretion will remain unchanged. It is possible that such mechanisms occurred as a result of the use of 10% mandelic acid and 25% gluconolactone applied manually. The use of AHA and PHA in our research significantly increased the level of hydration. The homeostasis of the epidermal barrier was maintained, hence the mechanisms leading to the increase in sebum secretion were not activated. Our research also noted a significant correlation between the level of hydration and sebum. As the hydration increased, the secretion of sebum decreased. This also explains the results obtained in the study related to sebum secretion. It is highly probable that as a result of the skin achieving an appropriate level of hydration, the sebaceous glands are regulated, and sebum secretion is maintained at a constant level.

The results obtained in our study indicate that 10% mandelic acid applied using ultrasound resulted in a significant increase in the amount of sebum secreted. Interestingly, in their study, Chilicka et al. [32]. proved that the application of green tea, bamboo extract, and 5% lactic acid with sonophoresis results in a reduction of skin eruptions and sebum production. The biological effect of ultrasound on tissues induces primary and secondary changes. The group of primary changes includes thermal, mechanical, and physicochemical phenomena [33]. Thermal reactions are manifested in an increase in the temperature of the place to which the treatment is subjected. The available literature data show that as a result of an increase in temperature by 1 °C, sebum secretion increases by 10% [34]. Thus, it is highly probable that as a result of the increase in temperature resulting from the use of ultrasound, a significant increase in sebum secretion could have occurred.

Analysis of the number of treatments in relation to the greatest improvement in skin condition can be important information helpful in determining the methodology of treatments using AHA and PHA. It is known that a single AHA therapy can cause exfoliation, but it is a series of treatments that are necessary to achieve a specific effect.

The largest statistically significant improvement in hydration in the A and B Groups occurred after the 4th treatment. These results may be an important element at the stage of planning the procedure methodology. They provide significant information regarding the effectiveness of the treatment. In order to achieve satisfactory results related to the increase in the level of hydration, a series of four treatments performed every 7 days is sufficient.

The largest statistically significant improvement in sebum secretion in the B and C Groups occurred after the second treatment. Satisfactory results in terms of sebum secretion on dry skin can be achieved after a series of two treatments at 7-day intervals. Perhaps the period of 14 days, which is the minimum time for the increase in sebum secretion, is related to the fact that the total duration of the sebum formation process also lasts 14 days [35]. The first treatment likely stimulates the sebaceous glands, but 14 days are necessary for sebum production.

The largest statistically significant reduction in erythema in Group B occurred after the sixth treatment. This means that in the case of erythema, to achieve satisfactory results, it is necessary to perform a series of six acid treatments, at weekly intervals.

Although AHAs and PHAs have been known and widely used for several decades, their mechanism of action has not been thoroughly studied. It is acknowledged that they affect the functional parameters of the skin, including the level of hydration, erythema, melanin production, and sebum secretion; nonetheless, the detailed stages of these reactions are not fully understood. AHA and PHA exfoliation is characterized by ease of performance, safety, and a relatively low irritating potential, and these treatments seem to be timeless. Mandelic acid and gluconolactone can be used alone or in combination with other chemical preparations. Properly selected treatment parameters and the appropriate form of application is an effective type of treatment for dehydrated skin, excessive erythema, and hyperpigmentation. The action of alpha-hydroxy acids, including mandelic acid, and polyhydroxy acids (gluconolactone) is multidirectional and their clinical effect depends on the method of application, concentration, pH, and the additional substance present in the chemical preparation.

5. Conclusions

Our study has shown that superficial chemical peels significantly alter the selected skin chemical parameters. Moreover, the use of mandelic acid and gluconolactone in low concentrations of higher pH constitutes the most effective method aimed at increasing the skin moisturization level. On the other hand, AHA and PHA applied via the method with ultrasounds do not affect the skin moisturization level, erythema, or skin pigmentation. According to our observations, the most effective procedure, based on the use of superficial chemical peels, and ultimately leading to a general enhancement of the skin parameters, proved to be the one involving a series of four procedures carried out in 7-day intervals.

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References

1. Liang, Y.; Su, W.; Wang, F. Skin Ageing: A Progressive, Multi-Factorial Condition Demanding an Integrated, Multilayer-Targeted Remedy. *Clin. Cosmet. Investig. Dermatol.* **2023**, *16*, 1215–1229. [CrossRef] [PubMed] [PubMed Central]
2. Augustin, M.; Kirsten, N.; Körber, A.; Wilsmann-Theis, D.; Itschert, G.; Staubach-Renz, P.; Zander, N. Prevalence, predictors and comorbidity of dry skin in the general population. *J. Eur. Acad. Dermatol. Venereol.* **2018**, *33*, 147–150. [CrossRef]
3. Fischer, T.C.; Perosino, E.; Poli, F.; Viera, M.S.; Dreno, B. Chemical peels in aesthe tic dermatology: An update 2009. *J. Eur. Acad. Dermatol. Venereol.* **2010**, *24*, 281–292. [CrossRef]
4. Wołosik, K.; Knaś, M.; Wacewicz, M.; Dmuchowska, P. Skuteczność terapii skojarzonej w redukcji blizn potrądzikowych–opis przypadków. *Dermatol. Rev. Dermatol.* **2013**, *100*, 102–109.
5. Marczyk, B.; Mucha, P.; Rotsztejn, H. Effect of chemical peelings the most often used in acne vulgaris. *Clin. Dermatol.* **2012**, *14*, 183–187.
6. Rubin, M.G. *Peelingi Chemiczne w Dermatologia Kosmetyczna*; Elsevier Urban & Partner: Wrocław, Poland, 2009; pp. 105–131.

7. Jin, L.; Hao, P.; Dong, S.; Bian, Y.; Yu, X. Antifeedant and Insecticidal Effects of Mandelic Acid on the Brown Planthopper Nilaparvata lugens Stål. *Z. Naturforschung C* **2011**, *66*, 499–506. [CrossRef]
8. Nowicka, D.; Ciszek, A.; Migasiewicz, A. Wpływ wybranych alfa-hydroksykwasów (AHA) na funkcje bariery ochronnej naskórka. *Dermatol. Estet* **2014**, *6*, 301–305.
9. Taylor, M.B. Summary of mandelic acid for the improvement of skin conditions. *Cosmet. Dermatol.* **1999**, *12*, 26–28.
10. Serafin, M. Peels—Acne and acne scars—Recommended protocols. *Dermatol. Cosmetol.* **2010**, *5*, 79–80.
11. Bernstein, E.F.; Brown, D.B.; Schwartz, M.D.; Kaidbey, K.; Ksenzenko, S.M. The polyhydroxy acid gluconolactone protects against ultraviolet radiation in an in vitro model of cutaneous photoaging. *Dermatol. Surg.* **2004**, *30*, 189–196.
12. Green, B.A.; Edison, B.L.; Wildnauer, R.H.; Sigler, M.R. Lactobionic acid and gluconolactone: PHAs for photoaged skin. *Cosmet. Dermatol.* **2001**, *14*, 24–28.
13. Rizer, R.L.; Turcotte, A.L.; Edison, B.; Outwater, S.; Trookman, N.S.; Ciociola, A.A.; Kohut, B.E. An evaluation of the tolerance profile of a complete line of gluconolactone-containing skin care formulations in atopic individuals. *Ski. Aging* **2001**, *9*, 18–21.
14. Green, B.A.; Briden, M.E. *Cosmeceuticals w Procedures in Cosmetic Dermatology*; Saunders Elsevier: Philadelphia, PA, USA, 2009; pp. 209–215.
15. Proksch, E.; Lachapelle, J. The management of dry skin with topical emollients–recent perspectives. *JDDG J. der Dtsch. Dermatol. Ges.* **2005**, *3*, 768–774. [CrossRef]
16. Dahl, M.; Dahl, A. 12% lactate lotion for the treatment of xerosis: A double-blind clinical evaluation. *Arch. Dermatol.* **1983**, *119*, 27–30. [CrossRef]
17. Chlebus, E.; Serafin, M. The chemical peels yesterday and today—Actual state of knowledge about chemoexfoliation (1). *Dermatol. Estet* **2015**, *17*, 102–107.
18. Berardesca, E.; Distante, F. Alpha hydroxyacids modulate stratum corneum barrier function. *Br. J. Dermatol.* **1997**, *137*, 934–938. [CrossRef]
19. Mitragotri, S.; Kost, J. Low-frequency sonophoresis: A review. *Adv. Drug Deliv. Rev.* **2004**, *56*, 589–601. [CrossRef]
20. Nowicki, A. Terapeutyczne zastosowanie ultradźwięków. *Ultrasonografia* **2008**, *8*, 9–17.
21. Mitragotri, S. Effect of bilayer disruption on transdermal transport of low-molecular weight hydrophobic solutes. *Pharm. Res.* **2001**, *18*, 1018–1023. [CrossRef]
22. Mańkowska, A.; Kasprzak, W. *Sonoforeza jako Transedrmalny System Terapeutyczny w Fizjoterapia w Kosmetologii i Medycynie Estetycznej*; Wydawnictwo Lekarskie PZWL: Warszawa, Poland, 2012; pp. 128–146.
23. Mańkowska, A.; Kasprzak, W. Metodyka Zabiegów Ultradźwiękowych. In *Fizykoterapia, Medycyna Uzdrowiskowa i SPA*; Wydawnictwo Lekarskie PZWL: Warszawa, Poland, 2010; pp. 243–250.
24. Ratajczak-Stefańska, V.; Maleszka, R.; Boer, M.; Kiedrowicz, M. Erythematotelangiectatic skin--diagnostic difficulties. *Ann. Acad. Med. Stetin.* **2009**, *55*, 58–65.
25. Woźniak, K. Czynniki warunkujące skuteczność działania biologicznego alfa- hydroksykwasów. *Dermatol. Estet* **2005**, *3*, 151–153.
26. Van Scott, E.J.; Yu, R.J. Alpha hydroxy acids: Procedures for use in clinical practice. *Cutis* **1989**, *43*, 222–228. [CrossRef] [PubMed]
27. Howard, P.C.; Sams, I.I.; Dennis, D.; Wamer, W.G. Alpha-hydroxy Acids: Consideration of the Biological Effects and Possible Role in Photococarcinogenesis. *J. Food Drug Anal.* **2002**, *10*, 258–261. [CrossRef]
28. Javaheri, S.M.; Handa, S.; Kaur, I.; Kumar, B. Safety and efficacy of glycolic acid facial peel in Indian women with melasma. *Int. J. Dermatol.* **2001**, *40*, 354–357. [CrossRef] [PubMed]
29. Garg, V.K.; Sinha, S.; Sarkar, R. Glycolic Acid Peels Versus Salicylic–Mandelic Acid Peels in Active Acne Vulgaris and Post-Acne Scarring and Hyperpigmentation: A Comparative Study. *Dermatol. Surg.* **2009**, *35*, 59–65. [CrossRef]
30. Knaggs, H. *Biologia Komórkowa Aparatu Mieszkowo-Łojowego w Trądzik, Diagnostyka i Leczenie*; Czelej Sp z o. o.: Lublin, Poland, 2009; pp. 11–44.
31. Fluhr, J.W.; Mao-Qiang, M.; Brown, B.E.; Wetz, P.W.; Crumrine, D.; Sundberg, J.P.; Feingold, K.R.; Elias, P.M. Glycerol regulates stratum corneum hydration in sebaceous gland deficient (asebia) mice. *J. Investig. Dermatol.* **2003**, *120*, 728–737. [CrossRef]
32. Chilicka, K.; Rogowska, A.M.; Rusztowicz, M.; Szyguła, R.; Yanakieva, A.; Asanova, B.; Wilczyński, S. The Effects of Green Tea (*Camellia sinensis*), Bamboo Extract (*Bambusa vulgaris*) and Lactic Acid on Sebum Production in Young Women with Acne Vulgaris Using Sonophoresis Treatment. *Healthcare* **2022**, *10*, 684. [CrossRef] [PubMed] [PubMed Central]
33. Mańkowska, A.; Kasprzak, W. *Biologiczne Oddziałaywanie Stymulacji Ultradźwiekowej w Fizjoterapia w Kosmetologii i Medycynie Estetycznej*; Wydawnictwo Lekarskie PZWL: Warszawa, Poland, 2012; pp. 131–134.
34. Nowicka, D. *Gruczoły Łojowe—Budowa i Funkcje w Choroby Łojotokowe Skóry*; KOSMED: Wrocław, Poland, 2011; pp. 5–9.
35. Downing, D.T.; Steward, M.E.; Wertz, P.W.; Strauss, J.S. On the mechanism of sebum secretion. *Arch. Dermatol. Res.* **1982**, *272*, 343–349. [CrossRef]