Efficacy of Mandelic Acid Serum on Acne Treatment and Recurrence Prevention

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1. Introduction

Acne vulgaris is a chronic inflammatory skin disorder that predominantly affects adolescents and primarily involves the pilosebaceous units of the face [1]. According to the Global Burden of Disease Study, acne has a prevalence of 9.4%, making it the eighth most prevalent disease worldwide. Beyond its physical manifestations, acne can significantly impact patients' mental health, often leading to anxiety, depression, and low self-esteem, thereby affecting their social interactions and overall quality of life [2].

The pathogenesis of acne is multifactorial, involving excessive sebaceous gland activity, follicular hyperkeratinization, microbial colonization (particularly by Propionibacterium acnes), and the release of inflammatory mediators. These factors collectively contribute to the formation of microcomedones, the precursors of all acne lesions [3].

Topical retinoids are considered the cornerstone of acne therapy. They exert their therapeutic effects through multiple mechanisms, including regulating keratinocyte proliferation and differentiation, exerting anti-inflammatory actions, and inhibiting microcomedone formation [4]. Although adapalene, a third-generation retinoid, has demonstrated significant clinical efficacy, approximately 10–40% of patients experience adverse effects such as skin dryness, peeling, and erythema, which can negatively impact long-term treatment adherence [5].

In recent years, an increasing body of research has highlighted the role of anti-comedonal skincare products targeting acne pathogenesis as adjunctive therapies. These products function by repairing the skin barrier, regulating the microbiota, and reducing sebum secretion, thereby supporting conventional treatments [6]. Furthermore, current evidence suggests that maintenance therapy combining adapalene with low-dose α- and β-hydroxy acids can significantly improve both inflammatory and non-inflammatory acne lesions, with good tolerability in patients with mild to moderate acne [7].

Mandelic acid (MA), an α-hydroxy acid (AHA), derives its name from the German word "Mandel" (almond) and is obtained through the hydrolysis of bitter almond extract. Its chemical formula is $HOCH(C_6H_5)COOH$, with a molecular weight of 152.14 g/mol. Compared to glycolic acid, a first-generation AHA, mandelic acid has a larger molecular size, resulting in slower skin absorption and reduced irritation potential. Mandelic acid exists as two optical enantiomers, which influence its pharmacological properties [8]. MA exhibits several beneficial effects relevant to acne treatment, including inhibition of epidermal keratinization, clearance of follicular plugs, antimicrobial activity, sebaceous gland regulation, improvement of pigmentation and atrophic scars, and prevention of acne recurrence.

Despite these promising properties, there is limited research on the use of mandelic acid-containing skincare products as an adjunct to adapalene in the treatment of mild to moderate acne. Therefore, this study aims to evaluate the safety and efficacy of mandelic

acid-containing skincare products, either as monotherapy or in combination with adapalene gel, during the early treatment and maintenance phases of mild to moderate acne. The findings are presented as follows:

2. Materials and Methods

2.1 Subjects

In this study, 41 patients with acne vulgaris of grade I-II according to the Pillsbury classification [8, 9] who visited the dermatology outpatient department and randomly divided into two groups.

2.1.1 Inclusion criteria

① Healthy males or females aged between 18 and 45 years old; ② Participants need to be able to understand the process and sign the consent form.

2.1.2 Exclusion criteria

① Pregnant or lactating women; ② Drug-induced acne and occupational acne caused by chemical substances; ③ Individuals with high sensitivity constitution; ④ Those using acne cosmetics or products in the past month; ⑤ Patients who have taken antibiotics, glucocorticoids, anti-androgen drugs such as spironolactone and other drugs for treating acne orally within 4 weeks before the experiment; or patients who have received physical treatment for acne; or patients who have undergone chemical peeling treatments such as salicylic acid and alpha-hydroxy acids; ⑥ Those who have taken oral retinoid drugs within 3 months before the experiment (acitretin drugs within 6 months); ⑦ Volunteers who are considered unsuitable to participate in this experiment according to clinical evaluation.

2.1.3 Withdrawal criteria

The experiment may be terminated if the subject experiences adverse reactions, is lost to follow-up, violates the research protocol, or there are other special circumstances. Subjects will also be withdrawn from the study if they cannot continue for any reason.

This study has been approved by the Ethics Committee (Approval No.202314), and all subjects have signed the informed consent form.

2.2 Methods

2.2.1 Product Usage Method and Frequency

Treatment Phase: After the start of the experiment, the control group used 0.1% adapalene gel, once a night, applied pointwise to the skin lesions, and only used basic moisturizing products in daily life. The treatment group, on the basis of the treatment of the control group, added skin care products containing mandelic acid . Specific usage method: Use it every morning and evening. After cleansing the face, take an appropriate amount of essence (about 1 dropper for the whole face) in the palm of your hand, and evenly spread it on the facial skin starting from the T-zone and moving from the inside out. Then, take 3-5 drops of essence and apply it pointwise to key local areas such as acne and closed comedones.

Maintenance Phase: Stop using the 0.1% adapalene gel. The control group uses basic moisturizing products in daily life. The treatment group continues to use skin care products containing mandelic acid on the basis of the control group.

The experimental design follows the principles of a single-center, randomized, and controlled trial. Tests and evaluations are conducted before use and at W2, W4 and W8 after

use respectively. During the experiment, continue to use the previous facial skin care products and do not change the skin care products three months before the experiment (to ensure that the state of the facial skin is basically stable during the experiment), and only replace similar products with the experimental products.

2.3 Evaluation Indicators

2.3.1 Quantitative Evaluation of Skin Physiological Indicators

Skin physiology was measured using the MPA10 system (Tewameter® TM300 for transepidermal water loss, Corneometer CM825 for hydration, Sebumeter SM815 for sebum) under controlled conditions (21±1°C, 50±10% humidity). Subjects cleaned their skin, rested for 30 minutes and were tested in the supine position. Facial imaging (VISIA-CR) analysed erythema (a* value) and porphyrins under standardised lighting, with Image-Pro Plus v7.0 software ensuring consistency.

2.3.2 Cyanoacrylate Skin Surface Stripping (CSSS)

According to the methods of Holmes[10], Fontao[11], and others, one drop of 2 - cyanoacrylate ethyl ester adhesive (CAS No. 7085 - 85 - 0, Sigma - Alrich, USA) is dropped onto the center of a pre - cleaned, fat - free glass slide. The slide is then quickly pressed onto the non - lesional skin surface in the center of the patient's forehead. After 1 minute, the slide is gently removed from the skin surface, taking care not to damage the stratum corneum and its comedones. The slide is placed under an ordinary optical microscope for calculation (magnification 40X). In 41 randomly selected areas of 0.5 cm^2, three items are counted: (1) the number of hair follicles, (2) the number of microcomedones, and (3) the type of microcomedones, which are ranked by size from level 0 - 4. From this, the following are calculated: (1) the percentage of hair follicles affected by microcomedones; (2) the microcomedone index (the proportion of microcomedones to the total number of hair follicles × the average size of microcomedones, with the size of microcomedones evaluated on a scale of 0 - 4).

2.3.3 Clinical Evaluation

(1) Physician Assessment

At each study visit, certified dermatologists performed standardized counts of facial acne lesions using magnified visual examination, categorizing lesions into non-inflammatory types (closed/open comedones), inflammatory types (papules and pustules), and total lesion counts.

(2) Subject Self-Assessment

Participants rated treatment outcomes using a 5-point Likert scale (5 = strongly agree; 1 = strongly disagree), with assessments covering the following domains: reduction in acne lesions, improvement in post-acne erythema/hyperpigmentation, regulation of sebum production, prevention of recurrence anf tolerability without irritation.

2.3.4 Safety Evaluation

Safety monitoring combined dermatologist-documented erythema, edema, and desquamation with patient-reported symptoms (pruritus, stinging, burning).

2.4 Statistical Analysis

Statistical analysis was performed with GraphPad Prism 10.4.0 using Shapiro-Wilk normality tests, two-way ANOVA for parametric data and Wilcoxon tests for non-parametric data (significance $P<0.05$). Agreement rates reflect percentages scoring ≥4 ('agree/strongly

agree') on Likert scales.

3. Results

3.1 Physician Assessment

3.1.1 Acne lesions count

（1）**Non-inflammatory types (closed/open comedones)**：Both experimental and control groups demonstrated a reduction trend compared to baseline. Significant improvements in w4 and w8 were observed in both groups（P＜0.05）, with the treatment group showing significantly improvement in w8 than the control group （P=0.038＜0.05）.

（2）**Inflammatory types (papules and pustules)**：The treatment group showed consistent improvements over time, especially at weeks 2 and 8 (P<0.05). The control group initially decreased but increased at week 8. No significant differences between the groups were found.

（3）**Total lesion counts:** The treatment group showed a decrease in lesions, while the control group's lesions worsened at W8. Significant improvements were seen in both groups at W4 and W8（P＜0.05）.

Table.1 Lesion counts (Noninflammatory lesion counts、Inflammatory lesion counts、Total lesion counts）

	Adjunctive therapy			Maintenance therapy
	Baseline	**W2**	**W4**	**W8**
Noninflammatory lesion counts				
Treatment	17.32±6.19	13.46±5.42	9.18±4.83*	8.18±4.21*#
Control	17.58±7.18	14.95±8.66	11.42±4.15*	12.05±4.79*
Inflammatory lesion counts				
Treatment	5.55±4.17	3.41±2.70*	3.64±2.87	2.68±2.30*
Control	4.26±4.15	3.53±3.67	3.58±4.83	4.32±5.64
Total lesion counts				
Treatment	22.86±6.93	16.86±6.74*	12.82±4.63*	10.86±5.84*
Control	21.84±6.38	18.47±9.34	15.00±6.64*	16.37±7.89*

Note: # was treatment group compared with control group; * was compared with Baseline（p<0.05）

3.1.2 Safety assessment

All 41 participants adhered strictly to the MA/adapalene protocols, with no adverse events reported. Vital signs remained normal and users reported a high level of comfort with MA products. Safety monitoring confirmed protocol compliance and physiological stability throughout the study.

3.2 Skin physiological indicators

（1）**TEWL**：Compared to baseline, the treatment group showed upward trends at W2 and W4 and a downward trend at W8. The control group showed upward trends at both W4 and W8. No statistically significant differences between or within groups were observed.

（2）**Corneometer**：Compared to baseline, both the treatment and control groups showed an upward trend at all three follow-up time points, with the treatment group showing a significant increase in hydration levels at week 8（P=0.035＜0.05）. There were no statistically significant differences between the two groups.

（3）**Sebumeter :** Compared to baseline, both the treatment and control groups showed a downward trend at W2 and W4, and an upward trend at W8. There were no statistically significant differences within or between groups.

Table 2. Skin physiological indicators (Transepidermal water loss, Stratum corneum hydration, Sebumeter)

	Adjunctive therapy			Maintenance therapy
	Baseline	**W2**	**W4**	**W8**
Transepidermal water loss				
Treatment	17.51±3.11	17.54±3.34	19.10±3.45	17.39±3.03
Control	18.50±2.82	17.86±2.59	20.30±3.27	18.83±3.73
Stratum corneum hydration				
Treatment	71.82±10.10	74.49±10.91	75.95±10.97	77.13±10.75*
Control	71.65±8.61	73.16±10.55	74.86±8.16	74.74±10.87
Sebumeter				
Treatment	103.80±52.05	91.68±51.92	88.86±36.86	93.46±38.43
Control	104.90±47.32	99.82±35.51	99.14±38.89	101.83±49.50

Note: * was compared with Baseline（$p<0.05$）.

3.3 VISIA-CR results

（1）**Erythema Area**：Erythema Area Index analysis showed decreasing trends in the treatment group at all three follow-up time points compared to baseline, while the control group showed decreases at W2 and W4, but an increase at W8. No significant between or within group differences were observed.

（2）**Porphyrin Index**：Analysis of the porphyrin index showed decreasing trends in the treatment group at all three follow-up time points relative to baseline, while the control group showed increasing trends at all time points. No statistically significant differences between or within groups were observed.

Table 3. VISIA-CR analysis

	Adjunctive therapy			Maintenance therapy
	Baseline	**W2**	**W4**	**W8**
Erythema area				
Treatment	9.11±1.66	8.84±1.93	8.64±1.46	8.65±1.56
Control	9.26±1.91	9.15±1.80	8.94±1.41	9.07±1.96
Porphyrin index（%）				
Treatment	13.95±7.13	13.61±5.95	12.80±6.28	13.42±6.02
Control	14.55±9.36	15.45±9.59	14.79±9.01	16.61±9.11

3.4 Microcomedone detection

（1）**Hair follicles with microcomedones (%)**：Compared to baseline, both the treatment and control groups showed a downward trend at all three follow-up time points.The treatment group showed statistically significant differences at W2, W4 and W8, whereas the control

group showed significance only at W4 (P＜0.05). A statistically significant difference between the groups was observed at W8.（P=0.001＜0.05）.

（2）Microcomdone index：The treatment and control groups showed a downward trend at all follow-up points, with the treatment group showing statistically significant results at W2, W4, and W8, whereas the control group showed significance only at W4 (P＜0.05). A statistically significant difference between the groups was observed at W8.（P=0.0005＜0.05）.

Table 4. Microcomdone analysis

	Adjunctive therapy			**Maintenance therapy**
	Baseline	**W2**	**W4**	**W8**
Hair follicles with microcomedones (%)				
Treatment	23.00±4.09	19.92±3.63*	17.25±4.55*	15.86±6.64*#
Control	24.07±4.19	22.08±6.02	20.01±5.55*	22.50±3.72
Microcomdone index				
Treatment	36.67±6.65	29.67±7.60*	24.31±8.13*	21.62±10.72*#
Control	39.89±8.20	36.89±12.49	30.88±9.79*	33.18±6.21

3.5 Subjective assessments

For subjective assessments, participants rated treatment efficacy using questionnaire scales, with the percentage of scores ≥4 used as the statistical indicator. Results showed that the treatment group had a higher proportion of patients reporting reduced acne count, improved post-acne hyperpigmentation, reduced sebum secretion and reduced acne recurrence compared to the control group. In addition, patient satisfaction progressively increased with prolonged use.

Table 5. Subject experience rating(%)

	W2	**W4**	**W8**
The number of pimples decreased after use			
Treatment	73.68	84.21	77.27
Control	54.55	63.64	63.16
Post-acne hyperpigmentation demonstrated clinical improvement			
Treatment	54.55	78.95	63.64
Control	47.37	72.73	57.89
Sebum secretion demonstrated a significant reduction			
Treatment	59.09	68.18	59.09
Control	52.63	63.16	52.63
Reduced recurrence of acne			
Treatment	40.91	63.16	72.73
Control	36.84	50.00	47.37
Tolerable and non-irritating			

Treatment	77.27	78.95	73.68
Control	73.68	72.73	72.73

4. Discussion

Functional skincare products effectively complement acne management alone or in combination with therapies [12], using alpha-hydroxy acids (e.g. MA) to reduce sebum/keratolysis and anti-C. acnes agents formulated in creams/cleansers [13]. Anti-comedogenic products are essential in the initial/maintenance phase for daily care, synergy and relapse prevention [14].This study is a two-phase randomised controlled clinical trial to evaluate the safety and efficacy of skin care products containing MA as adjuvant therapy, either alone or in combination with 0.1% adapalene gel. Clinical evaluations showed that during the treatment phase, the treatment group showed a downward trend in non-inflammatory, inflammatory and total lesion counts, with the treatment group demonstrating a superior magnitude of improvement compared to the control group. In the maintenance phase, the treatment group showed significantly better clearance efficacy for non-inflammatory and total lesions than the control group ($P < 0.05$), indicating its potential to reduce acne recurrence. Acids inhibit keratinisation, clear follicular plugs, regulate sebum and prevent recurrence, ideal for acne adjuvants [15]. Their gradual action increases safety. Garofalo V et al [16] demonstrated that a 4% benzoyl peroxide/1% MA cream improved mild acne lesions with hydration/sebum reduction. Dębowska RM et al [15] confirmed that 5-10% MA formulations safely reduced pustules/nodules. Combined with our findings, MA skincare works synergistically with pharmacotherapy in the treatment of mild to moderate acne, demonstrating sustained post-treatment efficacy.

Non-invasive assessments showed reduced transepidermal water loss (TEWL), increased stratum corneum hydration (SCH) and reduced sebum secretion in both the treatment and control groups, with greater improvements in the treatment group. Acne patients have impaired barrier function (increased sebum/TEWL/pH, decreased SCH) which correlates with the severity of acne. Topical retinoids, although effective against acne, compromise barrier integrity, allowing irritant penetration and inflammation via glandular hyperplasia/lipase/protease activation, culminating in follicular rupture, debris release and nodule/scar formation [17]. Post-treatment facial imaging showed reduced erythema (a*) and porphyrin indices in acne areas, particularly in the treatment group, suggesting potential anti-inflammatory and acne benefits of MA skin care, although not statistically significant. In addition to clinical assessments of acne improvement and non-invasive skin physiological assessments, this study used cyanoacrylate skin surface stripping (CSSS) to quantify the percentage of follicles affected by microcomedones and the microcomedone index. CSSS [18], a non-invasive technique using ethyl-2-cyanoacrylate for microcomedone analysis, identifies subclinical acne precursors in the follicular infundibulum [19]. Persistently low microcomedone indices correlate with clinical lesions, which are critical for relapse prevention [11].Both groups showed a reduction in microcomedones after treatment, but the treatment group achieved a sustained reduction during maintenance, preventing progression of acne lesions. The combination of MA and adapalene suppresses recurrence by inhibiting keratinisation, removing follicular plugs and regulating sebum production.

Safety evaluations showed no unexpected adverse events throughout the study, with all vital signs within normal physiological ranges and favourable product comfort ratings. These

results further demonstrate the safety profile and reliability of the formulation. Patient self-assessments showed that a higher proportion of participants in the treatment group reported reduced acne lesions, improved post-acne hyperpigmentation, reduced sebum secretion and lower recurrence rates compared to controls.

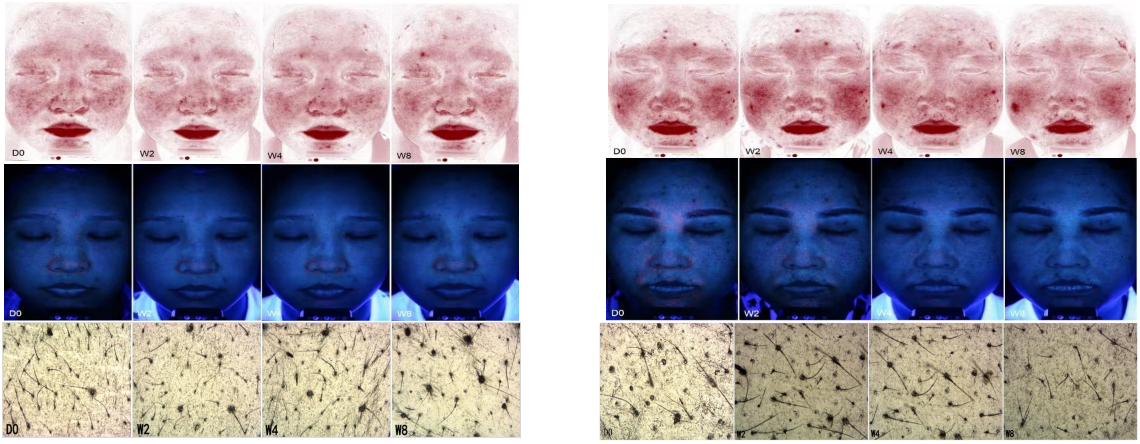

Figure 1. Typical pre- and post-treatment images of Erythema area, Porphyrin index, Microcomdone.(A:The control group; B:The treatment group)

5. Conclusions

The findings provide clinical evidence that mandelic acid serum contributes in the prevention of acne recurrence. Daily use mandelic acid serum after discontinued of adapalene can prevent the recurrence of acne lesions in 4 weeks. These results present a new strategy for acne skincare product development, emphasizing the potential for mandelic acid skincare formulations to enhace the clinical benefits of acne treatments.

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