Effectiveness of Microneedle Patch for Improvement of Under-Eye Skin

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Abstract

Skin aging represents an inherent biological progression affecting individuals of both male and female gender, typically manifesting as aesthetic concerns primarily focused on facial features. The etiology of skin aging is complex, involving various contributing factors. Wrinkling, for instance, arises from diminished collagen levels and decreased skin elasticity. The advancement of aging can significantly influence one's social perception and appearance. In this prospective study, a single-blind methodology was employed, and informed consent was obtained from all participants. Specifically, 36 healthy Thai women who exhibited mild to moderate under-eye wrinkles, as determined by a wrinkle severity scale, were recruited. The participants were requested to apply a newly designed microneedle patch to their faces for approximately five minutes nightly, twice a week. The treatments were applied to under-eye areas for 12 weeks, and assessments were conducted at baseline and at 4, 8, and 12 weeks. The microneedle patches demonstrated a notable improvement in the under-eye wrinkles grading, as evidenced by significant increases in participant-assessed scores. The microneedle patches create micro-injury and affect the development of collagen and tissue regeneration. Mild side effects such as erythema and pain were observed. The newly designed microneedle patches provided effective treatment for under-eye wrinkles with acceptable side effects. For individuals who are suffering from mild to moderate eye wrinkles, the microneedle patch can be an effective alternative. It has minimal side effects and can be used for a long time. The study was conducted solely on the microneedle patch, which means that further clinical trials with drug delivery methods will be conducted.

Keywords: *Under-eye Wrinkle, Microneedle Patch, Skin Rejuvenation*

1. Introduction

People commonly experience facial aging. The rise in the number of individuals seeking aesthetic procedures has been attributed to the condition's appearance, which is a result of sagging skin and the occurrence of fatty deposits. The under-eye issue is a source of concern as it contributes to an appearance of aging and an impression of fatigue. Maintaining a youthful appearance is important for people who are getting older (Koblenzer, 2003).

The use of microneedles for cosmetic procedures has been widely recognized and adopted. They can be used for various skin rejuvenation treatments and have been shown to successfully deliver the necessary chemicals to targeted areas. However, their precise mechanisms are still unknown. Two possible mechanisms are chemical delivery and the healing process of wounds by using micro-injuries (McCrudden et al., 2015; He et al., 2019). In multiple clinical trials, the use of microneedles has been able to reduce the appearance of wrinkles. According to a recent study in Thailand, 23 female Thai participants who were treated with the microneedle patch alone experienced significant improvements in their scores (Pruettijarai et al., 2022). The

microneedle patch can stimulate the growth of new cells and encourage neovascularization and the production of growth factors. In order to minimize the depth of the needles, we have developed a patch that can be used by patients at home.

The goal of this study is to analyze the novel design of this new microneedle patch. Thus, the patch was evaluated for its effectiveness and side effects.

2. Objectives

1) To investigate the therapeutic efficacy of a new microneedle patch design on skin rejuvenation in the under-eye areas based on the grading scale for under-eye wrinkles.
2) To investigate the side effects of microneedle patches.

3. Materials and Methods

3.1 Study Design and Participants

This prospective study was conducted using a single-blind approach. This research was reviewed by the Human Research Ethics Committee of Thammasat University (project number MTU-EC-OO-0-097/65). Informed consent was obtained from all participants. Thirty-six healthy Thai women participants who had mild to moderate under-eye wrinkles according to the wrinkles scale were recruited. The exclusion criteria were as follows: pregnancy and breastfeeding, history of energy-based device treatment within 1 year, history of laser therapy within 1 month, history of chemical peeling within 1 month, history of mesotherapy injection within 1 month, history of botulinum toxin or filler injection at under-eye areas within 1 year, and history of allergy or hypersensitivity to polymethylmethacrylate (PMMA) and monomer plastic since the microneedle patch is made from PMMA material, which is underlying that cosmetic and can affect their health condition, for example, systemic lupus erythematosus (SLE).

3.2 Microneedle patch

The microneedle patches were prepared by the nanoneedle research team, the Responsive Materials and Nanosensor Research Group at the National Nanotechnology Center, Thailand. The needles were made from polymethylmethacrylate (PMMA), a monomeric plastic material utilized in patch production. The microneedle (MN) array was fabricated on the fabric substrate via the photo-polymerization technique with a height of 350 μm and a density of 482 needles/cm^2, as shown in Figure 1(a). Moreover, the base diameter (w) is 200 μm, and the distance between the tips of the microneedles (d) is 644 μm. The shape of the microneedle patch was designed to cover the under-eye area, as seen in Figure 1(b).

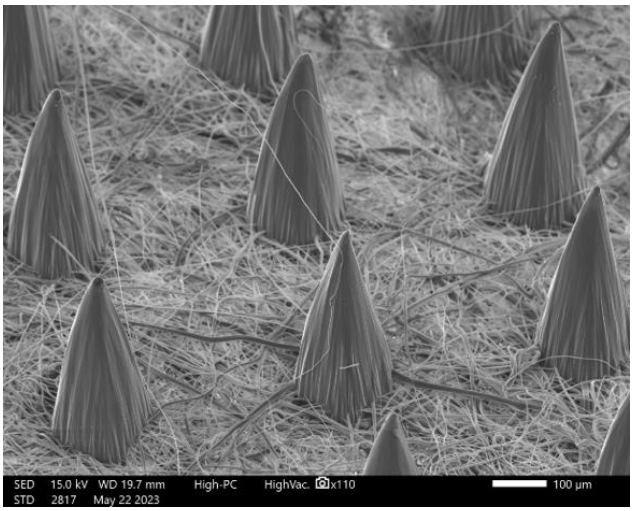

Figure 1(a) Microneedle array of 350 µm height with a density of 482 needles/cm^2

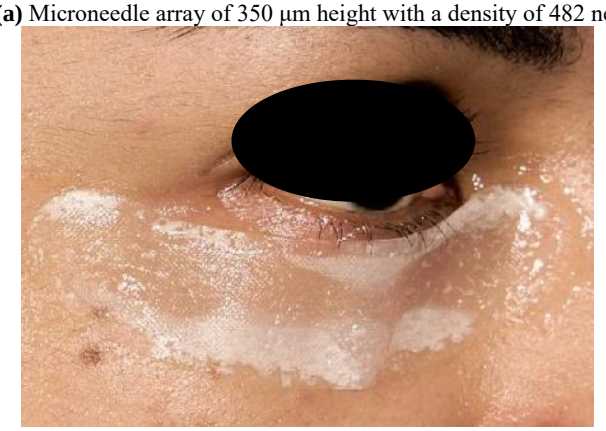

Figure 1(b) Microneedle patch applied under-eye.

3.3 Study protocol

The participants were requested to apply the microneedle patches with an average height (h) of 350 µm and a density of 482 needles/cm^2 to their faces in the under-eye area. All participants were informed of the study's risks and benefits. Prior to the treatment, a skin irritation test was performed by applying MN to each participant's forearm for five minutes. The participants were asked to wash their face with hibitane solution and apply the microneedle patch for around five minutes at night twice a week. The assessment was done every 4 weeks at baseline, 4, 8, and 12 weeks.

3.4 Outcome assessment

The primary outcome was the severity under the grading evaluated by two dermatologists, who were blinded to the study conditions, using the grading scale specifically designed for under-eye wrinkles (0 = no wrinkles, 1 = a few distinct, fine wrinkles, 1.5 = fine wrinkles with one or two moderate wrinkles, 2 = numerous distinct, fine wrinkles with a deep wrinkle confined to the medial side, 2.5 = numerous distinct, fine wrinkles

with a few moderate wrinkles, 3 = deep wrinkles on both medial and lateral sides and/or indistinct bags under-eyes, 3.5 = three or four deep wrinkles and/or distinct bags under-eyes, 4 = moderate wrinkles with numerous deep wrinkles) (Jang et al., 2022). The dermatologists' evaluations were based on photographs without specifying the participant or the week of assessment after the study was completed.

The secondary outcome was the participant satisfaction scores. Participants were asked to complete surveys with a 5-grade scale for the improvement of under-eye wrinkles: excellent (4), very improved (3), improved (2), no change (1), and worse (0).

Side effects were documented through post-study surveys, and if adverse events occurred, they were reported to the dermatologists immediately.

3.5 Statical analysis

All data are presented as mean. Statistical significance in all cases was considered at the *p*-value < 0.05. All statistical analyses were performed using SPSS. Generalized estimating equations were used.

4. Results and Discussion

4.1 Results

Thirty-six participants who fulfilled the inclusion criteria completed the study. The baseline characteristics and demographic data are shown in Table 1. The participants had a mean age of 34.25 ± 8.07 years, and all of them had mild to moderate under-eye wrinkles grades.

Table 1 Demographic Data

Demographic data	
Gender n, %	36 (100%)
Age, years (mean ± SD)	34.25 ± 8.07
Comorbid, n (%)	
No	30 (83.3%)
Hyperlipidemia	2 (5.6%)
Hypertension	1 (2.8%)
Allergic rhinitis	2 (5.6%)
Migraine	2 (5.6%)
Under-eye wrinkles grade, n (%)	
1	9 (25.0%)
1.5	15(41.7%)
2	9 (25.0%)
2.5	2 (5.6%)
3	1 (2.8%)
3.5	0
4	0

Note: The data shows the mean for the ages of the participants as mean ± SD.

At baseline, the results of the clinical assessment performed by two dermatologists using the grading scale of under-eye wrinkles were 1.61 ± 0.48. During a total of 12 weeks of research, the clinical responses showed improvement in the severity of wrinkles under the eyes (Figure 2 and Figure 3). Significant improvements in the severity of wrinkles were graded at different time intervals (Table 2).

The under-eye wrinkle grading showed a statistically significant decrease in the 8th week with a mean difference of 0.13 (*p*-value = 0.001). During the whole period, under-eye wrinkles were the most effectiveness with a mean difference of 0.15 at *p*-value < 0.001*.

Table 2 Mean grading and mean differences of grading under-eye wrinkles

	Under-eye wrinkles		
Weeks	Mean ± SD.	Mean Difference (95%CI)	*p*-value
0	1.61 ± 0.48		
4	1.6 ± 0.46	-0.01 (-0.08, 0.07)	0.859
8	1.49 ± 0.44	-0.13 (-0.2, -0.05)	0.001**
12	1.46 ± 0.45	-0.15 (-0.23, -0.08)	< 0.001**

Note: The data shows the mean grading of wrinkles represented as mean ± SD. Mean under-eye wrinkles grading was assessed by two independent dermatologists. The second column showing mean differences refers to wrinkles compared to the baseline at week 0. *p < 0.05. **p< 0.001.

The baseline score was 1. For the participants, the improvement rates were as follows: 0 = worse in any percentage, 1 = no improvement, 2 = improvement of 25% to 50%, 3 = improvement of 50% to 75%, and 4 = improvement of 75% to 100%. The participants' assessment suggested that there were statistical improvement.

Figure 2 Images of under-eye wrinkles of representative cases with the microneedle patch on the right side at (A) baseline, (B) 4, (C) 8, and (D) 12 weeks.

Significant improvements were recorded from weeks 2 to 12 in both under-eye wrinkles (*p*-value < 0.01). At 3 months, the improvement score was 79% (3.19 ± 0.58 *p*-value < 0.001*) (Figure 4).

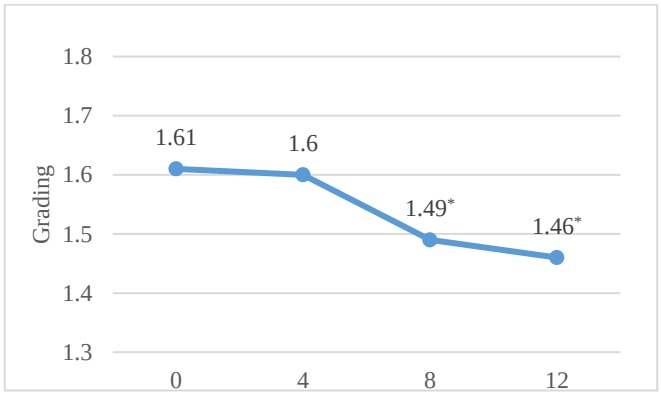

Figure 3 Under-eye wrinkle grading assessed by independent blinded dermatologists (*$p < 0.05$ compared to baseline)

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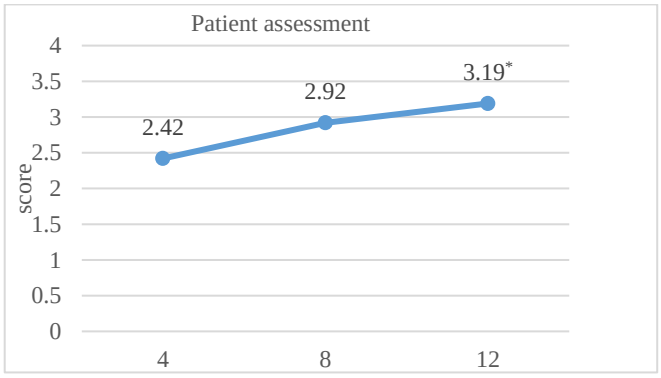

Figure 4 Participant satisfaction assessed by participants (*p < 0.05 compared to baseline)

There were no adverse effects during the application of the microneedle patch. According to the survey, the most common side effect was transient mild erythema and slight pain. The dermatologists did not notice any serious skin abnormalities during the time period of the study.

4.2 Discussion

The use of MN resulted in significantly better under-eye wrinkles grading. Moreover, the satisfaction scores were improved when evaluated by the participants themselves, corresponding to the grading results. This improvement was attributed to the microneedle patch's ability to stimulate the skin's natural healing process. In comparison with previous research, the use of magnesium microneedles for reducing under-eye wrinkles has shown improved results, consistent with our findings, in which the under-eye wrinkles were improved during 12 weeks (Jang et al., 2022). Simultaneously, a recent study in Thailand, in which 23 female Thai participants were treated with a microneedle patch and 1.8% hyaluronic acid on the right and left nasolabial folds, suggested that the patients who were treated with the microneedle patch alone experienced significant improvements in their scores (Pruettijarai et al., 2022). There were also no differences found in the improvement of wrinkles between the two groups. The microneedle patches affected the development of collagen and tissue regeneration. Another study, which was conducted on 34 Korean women, compared the effects of HA essences and microneedle patches on the appearance of crow's feet wrinkles. The microneedle patch was more effective than the HA essences in reducing wrinkles (Choi et al., 2017). In addition, it was revealed that the needling device can stimulate the healing process of post-needling wounds (Ramaut et al., 2018), and it can also stimulate the wound-healing process and increase the number of growth factors (McCrudden et al., 2015). The aggregation of neutrophils and the recruitment of other cells to the site of the injury can stimulate the production of various growth factors. These factors include vascular endothelial growth factor and growth factor beta (He et al., 2019; Bao et al., 2009; Guo & DiPietro, 2010). The ability to create scarless collagen is further enhanced by the post-needling cascade (Iosifidis & Goutos, 2019). This process triggers the formation of a physiologically based lattice-work collagen matrix, which is different from

the more stable collagen type III (Aust et al., 2008). Kim et al. (2014) noted that the use of microneedle patches can improve the appearance of various skin conditions.

The effects of the patches on the skin were also evaluated after they were applied. The dermatologists observed the skin's condition during each visit. Most of the participants experienced mild erythema during the survey. However, no severe adverse effects were observed.

5. Conclusion

The new microneedle patch design can be an alternative noninvasive treatment for people who have mild to moderate under-eye wrinkles. This new design can improve under-eye skin with minimal side effects. Since the study focused only on microneedle patches alone, further clinical trials and research on combination therapy with drug delivery methods should be conducted. Moreover, a long-term follow-up study to observe the longevity of the effectiveness is justified.

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