Clinical, Cosmetic and Investigational Dermatology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Efficacy and Safety Evaluation of Microneedling Combined with Tranexamic Acid-Arbutin Liquid Excipients in the Treatment of Melasma: A Retrospective Study

Mingli Zhang, Jincheng Ke, Yunhe Jiao, Li Ma

Dermatology Department, The Second Affiliated Hospital of Xiamen Medical College, Xiamen, People's Republic of China

Correspondence: Mingli Zhang, Email zhangmingli@xmmc.edu.cn

Background: The condition of melasma presents a complex pigmented skin disorder, characterized by increased production of melanin in the dermis. The main pathological change of melasma is photodamage to the dermis. The treatment of melasma is relatively complex, and tranexamic acid is a well-known drug, both topical and oral. While arbutin demonstrates notable skin brightening effects, it has not yet gained widespread clinical adoption. Microneedle therapy, however, not only enhances drug penetration and absorption but also stimulates tissue regeneration. Nevertheless, research on the combined application of tranexamic acid, arbutin, and microneedle therapy for melasma treatment remains limited.

Methods: A single-center retrospective dermatology study (Jan 2022–Jun 2023, n=27) evaluated microneedling plus tranexamic acid-arbutin solution for melasma. Medical records of 27 patients (3–6 months of treatment) were analyzed; efficacy was assessed via mMASI and PGA scores by two dermatologists, with side effect analysis.

Results: Before treatment, the average mMASI score of 27 patients with melasma was 5.426±2.128. After treatment with microneedling combined with tranexamic acid and arbutin liquid adjuncts, the mMASI score was 3.387±1.224, showing a mean decrease of 2.039±1.472 (37.58%). In terms of the PGA score, 20 patients achieved a score of 3 or higher (overall rate: 74.07%). The observed adverse reactions mainly include temporary erythema, burning sensation, petechiae (or/and ecchymosis), and skin dryness. The first two are more common but are mild in severity, with most cases resolving within hours; petechiae (or/and ecchymosis) and skin dryness are less common, and no cases of skin infection have been found.

Conclusion: Microneedling combined with tranexamic acid-arbutin liquid adjuvant treatment for melasma is feasible and well-tolerated. Its side effects are relatively few, but it is still recommended to appropriately adjust the treatment intervals, intensity, and density, or combine it with other methods to enhance efficacy.

Keywords: arbutin, melasma, Mesoderm therapy, microneedle, tranexamic acid

Background

Melasma is a chronic, stubborn, and highly recurrent pigmentation disorder that affects about 1% of the global population, especially women with darker skin. This condition not only severely affects appearance, but can also lead to anxiety, depression, and other mental health issues and social disabilities, thus reducing the quality of life for patients.

The pathogenesis of melasma is complex, and it is generally recognized that it is related to genetic factors, sex hormones, ultraviolet radiation, inflammation, oxidative stress damage, etc.[1] There exists a complex interaction between epidermal melanocytes, keratinocytes, fibroblasts, mast cells, and vascular endothelial cells.[1] These factors and cells ultimately lead to increased melanin synthesis in the skin through multiple pathways. New research shows that melasma lesions have a series of structural and functional changes in the dermis, epidermis and basement membrane zone, with elastic fiber degeneration, damage to the basement membrane zone, increased blood vessel formation, fibroblast

Received: 1 August 2025
Accepted: 5 November 2025
Published: 25 November 2025

senescence, and increased number of mast cells, and therefore melasma is considered to be a photo-aging disease of the skin, which is a new knowledge that will provide new ideas for the treatment of melasma.[2–4]

There are various treatment methods for melasma. Among the many therapies, tranexamic acid is a well-recognized medication due to its ability to inhibit melanin production, anti-inflammatory, and antioxidant effects, and it has been widely used in the clinical treatment of melasma, both orally and topically. However, due to the hydrophilic nature of tranexamic acid, it is difficult to penetrate the stratum corneum of the skin, hence new drug delivery methods are gradually being applied to the treatment of melasma with tranexamic acid, including traditional microneedles, dissolving microneedles, core-shell structured microneedles, hyaluronic acid-coated liposome nanogels, functionalized chitosan nanoparticles, etc. Nevertheless, some of the aforementioned methods have not yet been widely applied in clinical treatments.[5–8]

Microneedling is a recently developed drug delivery technology applied to treat various skin issues, including melasma. Existing studies indicate that microneedling is an effective adjunctive topical therapy for melasma.[9,10] However, there is limited evidence supporting its use alone;[11] combined treatments are often the preferred choice, including microneedling combined with tranexamic acid, platelet-rich plasma, and others. A systematic review found that the combination of microneedling and tranexamic acid is more effective than monotherapy in improving melasma lesions.[12] However, there is currently no one-size-fits-all treatment, and the treatment cycle is long, making it still challenging to completely change or reverse pigmentation disorders.[13]

Therefore, we have noticed another whitening product, arbutin, which can reduce the activity of tyrosinase while inhibiting the maturation of melanocytes, and it is non-toxic.[14] Research shows that the combination of a non-invasive home radiofrequency device and arbutin cream can effectively improve melasma.[15] Another study shows that the local application of arbutin nano vesicle hydrogel is an effective method for the treatment of melasma.[16]

Based on the above information, we focused on the method of treating melasma with microneedles combined with tranexamic acid-arbutin liquid excipients, which is a less commonly used method in the past. We used a retrospective analysis approach to evaluate the efficacy and safety of microneedle-tranexamic acid-arbutin as an inseparable whole in the treatment of melasma.

Methods

This is a retrospective case series study where we collected and analyzed the medical records of 27 patients with melasma who visited our hospital's dermatology department from January 2022 to June 2023. Inclusion criteria: received microneedling combined with tranexamic acid-arbutin liquid adjuvant treatment and adhered to the treatment for 3–6 months, complete medical records, clear photographs, male and female. Among the exclusion criteria, we excluded patients with melasma who received other treatments, patients with incomplete data, unclear photographs or those who might affect the assessment, concomitant immune diseases, tumors, facial scarring, oral medications, and outdoor workers. This study selected a total of 31 cases that met the inclusion criteria, and 4 cases were excluded according to the exclusion criteria: 1 case of outdoor worker (due to high UV exposure risk which may have an unmeasurable impact on treatment), 1 case of facial scar, and 2 cases of unclear imaging. The remaining 27 cases were included in the study.

This study complies with the requirements of the Declaration of Helsinki and has been approved by the Ethics Committee of the Second Affiliated Hospital of Xiamen Medical College (No. 2024090). Due to the anonymization of data and the minimal risk of the research, clinical informed consent is waived. Additionally, the patient in Figure 1 has provided written informed consent for the publication of the image.

Treatment process: Before the first treatment, patients are required to sign an informed consent form. Photographs are taken before each treatment for documentation, and adverse reactions after the last treatment are recorded. The specific steps for microneedling treatment are as follows: After cleansing the face, apply a 5% compound lidocaine cream externally for about 45 minutes. After cleansing the face, apply 5% compound lidocaine cream externally for about 45 minutes. After cleaning the surface anesthetic, perform three iodine disinfections, and wash with 0.9% sodium chloride solution to remove iodine. Immediately apply a tranexamic acid-arbutin liquid supplement (a mixed liquid with production license, containing 5% tranexamic acid and 1% arbutin) to the area of chloasma lesions. Then, roll the microneedle with appropriate force (manual microneedle roller, specifications: 0.25×0.5mm or 0.25×1.0mm), while continuing to apply the liquid supplement and gently massage to promote absorption until the skin shows slight redness

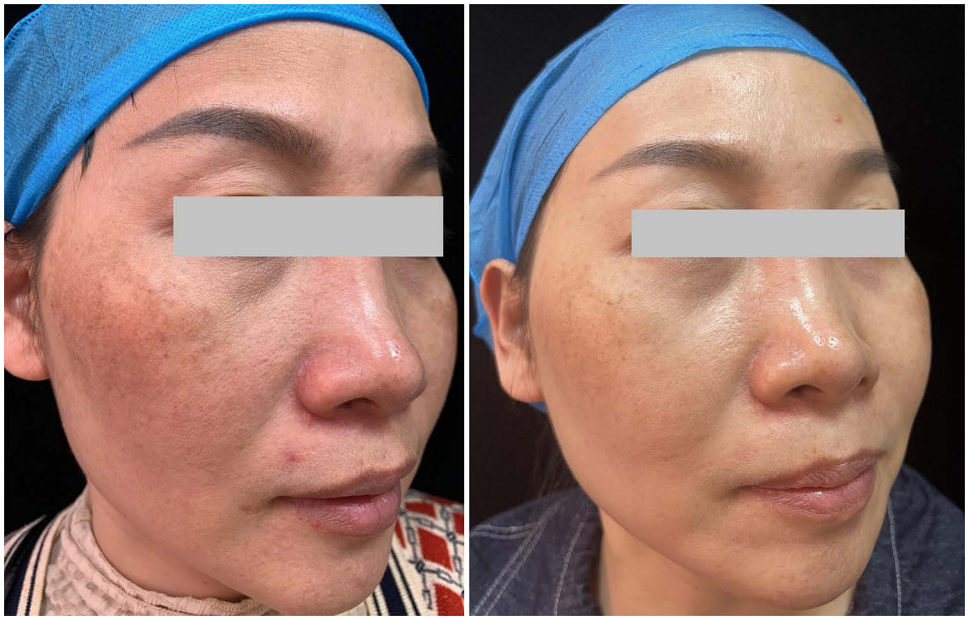

Figure 1 Before-and-after photos of a female patient.
Note: The left side of the picture shows the treatment before, and the right side shows the treatment after.

(end of treatment). Generally, repeating the microneedling treatment three times can achieve a slight redness of the skin. Immediately after treatment, apply a medical cold compress for cooling for half an hour, and no special medications are used post-treatment. Treatment is done once every two weeks for a duration of 3–6 months. Daily care includes routine moisturizing and sun protection measures.

Data organization and analysis: Two independent (not involved in the treatment) dermatologists reviewed the patient's before and after photos and assessed the improvement of melasma before and after treatment using the Modified Melasma Area and Severity Index (mMASI) score and the PGA score,[17–19] Before calculating mMASI, it is necessary to complete the assessment of the lesion area and the severity score of darkness. Area of involvement is rated on a scale from 0 to 6: 0 indicates absent; 1, <10%; 2, 10%–29%; 3, 30%–49%; 4, 50%–69%; 5, 70%–89%; 6, 90%–100%; Darkness rated 0–413: 0 indicates absent; 1, slight; 2, mild; 3, marked; 4, severe. The mMASI Score ranges from 0 to 24 and consists of four scores for the forehead, left and right face and chin. mMASI score =0.3A(f) D (f)+0.3 A (lb) D (lb)+0.3 A (rb) D (rb)+0.1A(m) D (m). Where A represents the cutaneous lesion area score, D represents the darkness score, f represents the Frontal Region, lb represents the left buccal region, rb represents the right buccal region, and m represents the mental region.

The average of these 2 dermatologist scores was used as the final score for this patient. Statistical analyses were performed using SPSS software, version 23. Measurements (mMASI scores) were confirmed to be normally distributed by the Kolmogorov–Smirnov test ($P > 0.05$ was considered to be normally distributed), and the paired-samples *t* test was used, with a difference of $P \leq 0.05$ considered to be statistically significant.

Results

Twenty-seven patients (2 males and 25 females) with melasma who met the inclusion criteria were included in this study. Their basic characteristics such as age, disease duration and skin type are detailed in Table 1. The mean age of the patients was 36.96 ± 4.381 years, with an age range of 29 to 45 years, and the mean disease duration was 2.937 ± 1.896 years, with a fluctuating range of 0.5 to 8.5 years.

After Kolmogorov–Smirnov test, we found that mMASI scores of all patients before and after treatment were normally distributed (p=0.2, p=0.068).

Table 1 Basic Characteristics

Patient Characteristics	n	%
Age (years)	Mean±SD 36.96±4.381	
≤30	2	7.41
31-39	18	66.67
≥40	7	25.93
Gender		
Male	2	7.41
Female	25	92.59
Duration of disease	Mean±SD 2.937±1.896	
≤1	4	14.81
1-3	11	40.74
≤1	12	44.44
Fitzpatrick skin type		
III	21	77.78
IV	6	22.22
Site of lesion		
Frontal Region	5	18.52
Buccal Region	27	100.00
Mental Region	1	3.70

Abbreviations: n, number of patients; %, percentage, Mean: average, SD: standard deviation.

The distribution of pigmentation in the 27 patients before treatment is detailed in Table 2, in which all of them showed involvement in the cheeks, and most of them had extensive lesions, with 18 patients (66.67%) having a pigmented area of 50% or more. In addition, there was one case of involvement in the chin region with lesion area of more than 30%. The frontal region was involved in five cases, one of which affected almost the entire frontal region, while the other four were limited to less than 10% of the area.

Table 2 Pigmentation Distribution and Darkness Severity of Melasma Before Treatment

Score	Area of Involvement, n (%)	Darkness Severity, n (%)
1		
Frontal Region	2 (7.41)	4 (14.81)
Buccal Region	1 (3.70)	3 (11.11)
Mental Region	0 (0)	0 (0)
2		
Frontal Region	2 (7.41)	1 (3.70)
Buccal Region	3 (11.11)	13 (48.15)
Mental Region	0 (0)	1 (3.70)
3		
Frontal Region	0 (0)	0 (0)
Buccal Region	5 (18.52)	11 (40.74)
Mental Region	1 (3.70)	0 (0)
4		
Frontal Region	0	0 (0)
Buccal Region	8 (29.63)	0 (0)
Mental Region	0 (0)	0 (0)

(*Continued*)

Table 2 (Continued).

Score	Area of Involvement, n (%)	Darkness Severity, n (%)
5		
Frontal Region	0 (0)	–
Buccal Region	9 (33.33)	–
Mental Region	0 (0)	–
6		
Frontal Region	1 (3.70)	–
Buccal Region	1 (3.70)	–
Mental Region	0 (0)	–

Abbreviations: n, number of patients; %, percentage.

The severity of pre-treatment darkness is presented in Table 2. Among the 27 cases, the darkness on the cheek was predominantly mild, marked or severe (24 cases,88.89%), while only 3 cases (11.11%) exhibited slight darkness. Regarding the forehead, 4 cases showed slight darkness, whereas another case displayed mild darkness. The darkness on the chin was classified as slight.

The mean mMASI score before treatment was 5.426± 2.128, and after treatment the mMASI score was 3.387±1.224, with a mean decrease of 2.039±1.472 (a decrease of 37.58%, 95% CI: 1.466–2.612, effect size Cohen's d=0.96). The difference between pre- and post-treatment mMAS scores was statistically significant (t=7.196, P=0). mMAS scores decreased in 22 cases (81.48%) after treatment, 4 cases (14.81%) had no change in mMAS score before and after treatment and 1 case (3.70%) had an increase in mMAS score after treatment. Figure 1 illustrates a typical case in which the severity of facial hyperpigmentation improved significantly after six months of treatment, but the area of the lesions was not reduced.

When 27 patients were evaluated for PGA, the following scenarios emerged: 2 (7.41%) received a score of 2, 7 (25.93%) received a score of 3, 11 (40.74%) received a score of 4, and 6 (22.22%) received a score of 5, whereas only 1 person received a score of 6 (3.70%). According to Figure 2, the number of patients who received a score of 2–4 out of these cases was as high as 20 (overall rate of 74.07%).

Immediately after treatment, all patients experienced erythema and some reported a burning sensation. In most cases, the erythema and burning could be reduced within a few hours by applying cold compresses. However, a few patients sustained erythema for 2–3 days. Bleeding spots, petechiae and dry skin are rare. There were no cases of infectious skin diseases. The occurrence of all adverse reactions is shown in Table 3.

Discussion

Microneedle is a micron-sized needle with a height of about 10–2000 microns and a width of 10–50 microns, which can penetrate the epidermis and enter the deeper layers, providing precise in-situ treatment with little invasive damage and little or no pain.[20–22] In recent years, it has been gradually emphasized and applied. Micro-needles form tens of thousands of tiny pores on the skin, which is conducive to the smooth transdermal absorption of drug molecules, and quickly reaches the target tissues to play a role, which is an effective transdermal drug delivery technology.[23,24] At the same time, these numerous tiny physical injuries will induce a wound healing cascade, start the skin regeneration and repair process, and induce elastin and collagen expression and deposition.[9,25] It has shown good efficacy in atrophic scars, actinic dermatoses, alopecia and hyperpigmentation disorders with mild side effects.[9,11]

Microneedling, as an adjunctive drug delivery route, is often used in combination with medications, especially in the topical treatment of melasma. A meta-analysis of 12 studies on microneedling showed that the combination of microneedling improved the severity of melasma better than topical medication alone, making microneedling an effective adjunctive treatment for melasma.[10] Microneedling avoids the low bioavailability and poor compliance of oral medications and enhances the action of the medication in the target tissues.[26,27]

In terms of drug combinations, tranexamic acid is the first choice for treating melasma, as both its topical and oral administration have been proven to be significantly effective. However, arbutin is also noteworthy; this whitening

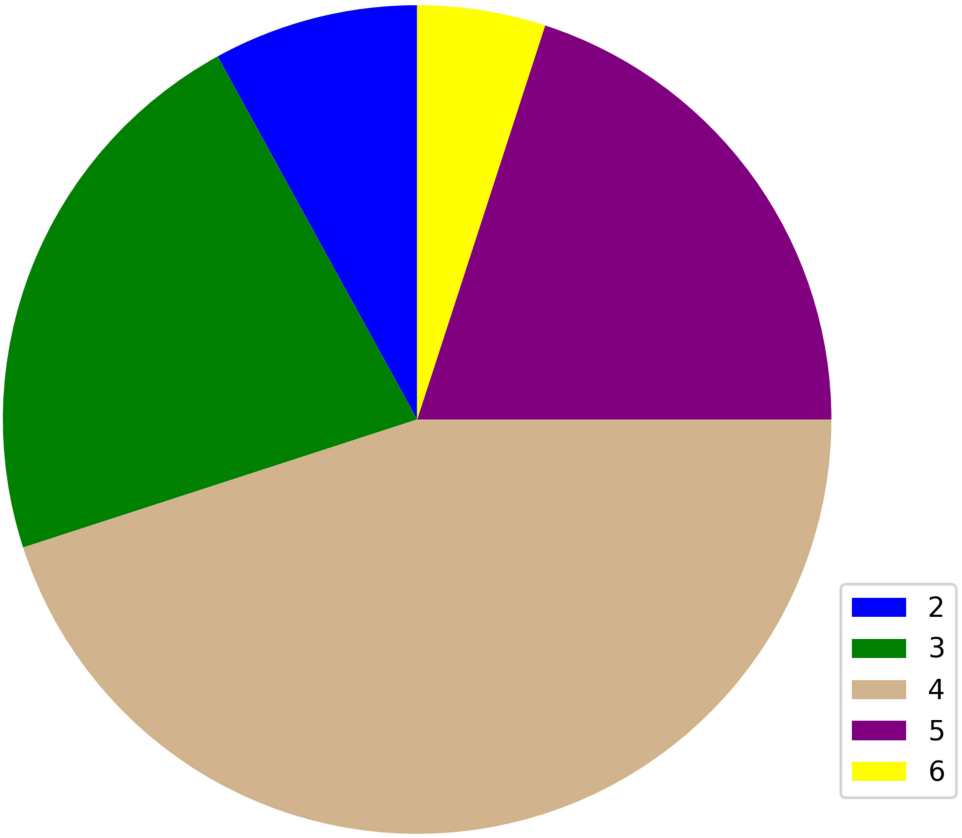

Figure 2 Percentage of PGA scores.
Notes: A score of 2 indicates 75–89% improvement, 3 indicates 50–74% improvement, 4 indicates 25–49% improvement, 5 indicates less than 25% improvement, and 6 is worse than before treatment.

ingredient can effectively reduce melanin production by inhibiting tyrosinase activity and exerting antioxidant effects, and it has been used alone in the treatment of melasma.[8,28,29]

At the same time, the multiple micro-injuries of micro-needling initiate the body's re-repair mechanism and promote collagen and elastin regeneration, which facilitates the repair of damage to the dermis as well as the basement membrane, which is very beneficial to the treatment of melasma.[30,31] More and more studies have concluded that the main pathological mechanism of melasma is dermal aging, and this alteration continues to release signals that promote melanin synthesis, contributing to the maintenance of melasma symptoms.[32]

In our study, the treatment of melasma by microneedling combined with drugs showed a decreasing trend in mMASI scores in 81.48% of the patients, with an average decrease of 37.58%, demonstrating a favorable therapeutic effect. This is mainly due to the combined effects of two types of whitening agents and the micro-needling technique that promotes the regeneration of collagen and elastin, effectively inhibiting melanin production and repairing skin aging damage. The adverse effects of the treatment were few and mild and subsided within a short period of time, which is in high agreement with the literature and indicates an excellent safety profile.[9,33]

Table 3 Occurrence of Adverse Reactions

Adverse Reactions	Erythema	Burning Sensation	Morrhagic Spots, Ecchymosis	Dry Skin	Infectious Dermatosis
n	27	19	5	3	0
%	100.00	70.37	18.52	11.11	0

Abbreviations: n, number of patients; %, percentage.

However, this study also observed that one patient experienced worsened condition and an increase in mMASI score after treatment. But after three local injections of platelet-rich plasma therapy, the patient's condition improved significantly. The analysis showed that the patient's erythema faded relatively slowly after each treatment, which was speculated to be related to the high intensity or density of microneedling. Additionally, her continuous makeup application and removal during the treatment may have damaged the skin barrier function, thereby offsetting the reparative effects of microneedling therapy.

During treatment procedures, we recommend that the length and diameter of the microneedles should not be too large, the treatment intensity should be gentle, the frequency should not be high, and scientific daily skin care is necessary.

Our research shows that for melasma, microneedling combined with tranexamic acid and arbutin, as a physical therapy integrated with two whitening agents (especially arbutin, which is currently less commonly used clinically), is worth attention. This combined therapy may be more effective in improving melasma or reducing adverse reactions when used in conjunction with platelet-rich plasma treatment. However, due to pain, patients often need topical anesthetics, which increases their financial burden and the risk of facial skin intolerance to the anesthetic, all of which limit the clinical use of this therapy.

During the follow-up of the patients, we observed that a portion of them experienced a relapse of their condition, with the earliest recurrence occurring 3 months after treatment cessation, although the severity was milder than before treatment. Due to incomplete follow-up data, this study did not analyze the follow-up data, which is also one of our regrets and limitations. Additionally, this study had a relatively small sample size, excluded outdoor workers (which may lead to selection bias), had a short observation period, and lacked stratified analysis, all of which affected the depth of the study. Furthermore, this study treated microneedles - tranexamic acid - arbutin as an indivisible whole to evaluate its efficacy and safety for melasma, which led to insufficient exploration of the treatment effects on melasma when using microneedles, tranexamic acid, and arbutin individually or in pairs, representing another limitation of this study. We will continue to pay attention to clinical research in this area and report our research results in a timely manner.

Conclusion

Microneedle therapy combined with tranexamic acid and arbutin liquid auxiliary agents for the treatment of melasma is feasible and well-tolerated. However, analysis shows that the mMASI scores of most patients only decreased by 37.58% after treatment, indicating a limited effect on improving pigmentation, and the improvement in lesion area is also minimal. The proportion of patients achieving a PGA score of 4 is 40.74%, suggesting that there is still room for improvement in pigmentation inhibition. Therefore, further research is needed to explore adjustments, including altering treatment intervals, increasing treatment frequency, optimizing treatment intensity, or combining with other therapies.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Sarkar R, Bansal A, Ailawadi P. Future therapies in melasma: what lies ahead? *Indian J Dermatol Venereol Leprol*. 2020;86(1):8–17. Erratum in: Indian J Dermatol Venereol Leprol. 2020 Sep-Oct;86(5):608. doi: 10.4103/0378-6323.292501. PMID: 31793496. doi:10.4103/ijdvl.IJDVL_633_18
2. Ali L, Al Niaimi F. Pathogenesis of melasma explained. *Int J Dermatol*. 2025;64(7):1201–1212. PMID: 40022484. doi:10.1111/ijd.17718
3. Passeron T, Picardo M. Melasma, a photoaging disorder. *Pigm Cell Melanoma Res*. 2018;31(4):461–465. PMID: 29285880. doi:10.1111/pcmr.12684
4. Kwon SH, Na JI, Choi JY, Park KC. Melasma: updates and perspectives. *Exp Dermatol*. 2019;28(6):704–708. PMID: 30422338. doi:10.1111/exd.13844
5. Xing M, Wang X, Zhao L, et al. Novel dissolving microneedles preparation for synergistic melasma therapy: combined effects of tranexamic acid and licorice extract. *Int J Pharm*. 2021;600:120406. PMID: 33711468. doi:10.1016/j.ijpharm.2021.120406
6. Jia T, Geng Y, Shao H, et al. A core-shell structured microneedle patch with adjustable release of kinetically for the treatment of melasma. *Adv Healthc Mater*. 2025;9:e02052. PMID: 40926406. doi:10.1002/adhm.202502052
7. Liu Y, Han Y, Zhu T, et al. Targeting delivery and minimizing epidermal diffusion of tranexamic acid by hyaluronic acid-coated liposome nanogels for topical hyperpigmentation treatment. *Drug Deliv*. 2021;28(1):2100–2107. PMID: 34596008; PMCID: PMC8491700. doi:10.1080/10717544.2021.1983081
8. Hatem S, Elkheshen SA, Kamel AO, et al. Functionalized chitosan nanoparticles for cutaneous delivery of a skin whitening agent: an approach to clinically augment the therapeutic efficacy for melasma treatment. *Drug Deliv*. 2022;29(1):1212–1231. PMID: 35403519; PMCID: PMC9004510. doi:10.1080/10717544.2022.2058652
9. Iriarte C, Awosika O, Rengifo-Pardo M, Ehrlich A. Review of applications of microneedling in dermatology. *Clin Cosmet Invest Dermatol*. 2017;10:289–298. PMID: 28848356; PMCID: PMC5556180. doi:10.2147/CCID.S142450

10. Bailey AJM, Li HO, Tan MG, Cheng W, Dover JS. Microneedling as an adjuvant to topical therapies for melasma: a systematic review and meta-analysis. *J Am Acad Dermatol*. 2022;86(4):797–810. PMID: 33857549. doi:10.1016/j.jaad.2021.03.116
11. Wu SZ, Muddasani S, Alam M. A systematic review of the efficacy and safety of microneedling in the treatment of melasma. *Dermatol Surg*. 2020;46(12):1636–1641. PMID: 32897944. doi:10.1097/DSS.0000000000002763
12. Olugbade ID, Negbenebor NA. The use of tranexamic acid and microneedling in the treatment of melasma: a systematic review. *Cutis*. 2024;114 (2):E15–E23. PMID: 39298769. doi:10.12788/cutis.1080
13. Neagu N, Conforti C, Agozzino M, et al. Melasma treatment: a systematic review. *J DermatolTreat*. 2022;33(4):1816–1837. PMID: 33849384. doi:10.1080/09546634.2021.1914313
14. Searle T, Al-Niaimi F, Ali FR. The top 10 cosmeceuticals for facial hyperpigmentation. *Dermatol Ther*. 2020;33(6):e14095. PMID: 32720446. doi:10.1111/dth.14095
15. Zhang L, Zhao Q, Che Q, et al. Effectiveness and safety of combined use of home-based radiofrequency device and arbutin cream in melasma and facial rejuvenation. *J Cosmet Dermatol*. 2025;24(2):e70007. PMID: 39918262; PMCID: PMC11804296. doi:10.1111/jocd.70007
16. Hatem S, Kamel AO, Elkheshen SA, et al. Nano-vesicular systems for melanocytes targeting and melasma treatment: in-vitro characterization, ex-vivo skin retention, and preliminary clinical appraisal. *Int J Pharm*. 2024;665:124731. PMID: 39306205. doi:10.1016/j.ijpharm.2024.124731
17. Abou-Taleb DA, Ibrahim AK, Youssef EM, Moubasher AE. Reliability, validity, and sensitivity to change overtime of the modified melasma area and severity index score. *Dermatol Surg*. 2017;43(2):210–217. PMID: 27930379. doi:10.1097/DSS.0000000000000974
18. Wong CSM, Chan MWM, Shek SYN, Yeung CK, Chan HHL. Fractional 1064 nm picosecond laser in treatment of melasma and skin rejuvenation in asians, a prospective study. *Lasers Surg Med*. 2021;53(8):1032–1042. PMID: 33544930. doi:10.1002/lsm.23382
19. Farshi S, Mansouri P. Study of efficacy of microneedling and mesoneedling in the treatment of epidermal melasma: a pilot trial. *J Cosmet Dermatol*. 2020;19(5):1093–1098. PMID: 32196865. doi:10.1111/jocd.13369
20. Hao Y, Li W, Zhou X, Yang F, Qian Z. Microneedles-based transdermal drug delivery systems: a review. *J Biomed Nanotechnol*. 2017;13 (12):1581–1597. PMID: 29490749. doi:10.1166/jbn.2017.2474
21. Zheng B, Li Q, Fang L, et al. Microorganism microneedle micro-engine depth drug delivery. *Nat Commun*. 2024;15(1):8947. PMID: 39414855; PMCID: PMC11484856. doi:10.1038/s41467-024-53280-8
22. Boca A, Fanian F, Smit R, et al. Evaluation of the performance and safety of a new micro-needle technology in comparison with the classic needle on the antiaging effects of a biorevitalizing solution: a randomized split face/neck study. *J Cosmet Dermatol*. 2024;23(12):3974–3985. PMID: 39356623; PMCID: PMC11626338. doi:10.1111/jocd.16547
23. Nguyen HX, Nguyen CN. Microneedle-mediated transdermal delivery of biopharmaceuticals. *Pharmaceutics*. 2023;15(1):277. PMID: 36678906; PMCID: PMC9864466. doi:10.3390/pharmaceutics15010277
24. Turner JG, White LR, Estrela P, Leese HS. Hydrogel-forming microneedles: current advancements and future trends. *Macromol Biosci*. 2021;21(2): e2000307. PMID: 33241641. doi:10.1002/mabi.202000307
25. McCrudden MT, McAlister E, Courtenay AJ, González-Vázquez P, Singh TR, Donnelly RF. Microneedle applications in improving skin appearance. *Exp Dermatol*. 2015;24(8):561–566. PMID: 25865925. doi:10.1111/exd.12723
26. Ahmed Saeed Al-Japairai K, Mahmood S, Hamed AS, et al. Current trends in polymer microneedle for transdermal drug delivery. *Int J Pharm*. 2020;587:119673. PMID: 32739388; PMCID: PMC7392082. doi:10.1016/j.ijpharm.2020.119673
27. Hou X, Li J, Hong Y, et al. Advances and prospects for hydrogel-forming microneedles in transdermal drug delivery. *Biomedicines*. 2023;11 (8):2119. PMID: 37626616; PMCID: PMC10452559. doi:10.3390/biomedicines11082119
28. Xu H, Li X, Xin X, et al. Antityrosinase mechanism and antimelanogenic effect of arbutin esters synthesis catalyzed by whole-cell biocatalyst. *J Agric Food Chem*. 2021;69(14):4243–4252. PMID: 33821640. doi:10.1021/acs.jafc.0c07379
29. Boo YC. Arbutin as a skin depigmenting agent with antimelanogenic and antioxidant properties. *Antioxidants*. 2021;10(7):1129. PMID: 34356362; PMCID: PMC8301119. doi:10.3390/antiox10071129
30. Hou A, Cohen B, Haimovic A, Elbuluk N. Microneedling: a Comprehensive Review. *Dermatol Surg*. 2017;43(3):321–339. PMID: 27755171. doi:10.1097/DSS.0000000000000924
31. Alster TS, Graham PM. Microneedling: a review and practical guide. *Dermatol Surg*. 2018;44(3):397–404. PMID: 28796657. doi:10.1097/ DSS.0000000000001248
32. Han HJ, Kim JC, Park YJ, Kang HY. Targeting the dermis for melasma maintenance treatment. *Sci Rep*. 2024;14(1):949. PMID: 38200171; PMCID: PMC10781782. doi:10.1038/s41598-023-51133-w
33. Gowda A, Healey B, Ezaldein H, Merati M. A systematic review examining the potential adverse effects of microneedling. *J Clin Aesthet Dermatol*. 2021;14(1):45–54. PMID: 33584968; PMCID: PMC7869810.