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BACKGROUND Microde rmabrasion is a widely performed skin re juve na tion procedure. It can partly ablate and homogenize the stratum corneum (SC) layers.

OBJECTIVE The effe ct of microderma brasion tre atment on the skin pe rmea tion of hydrophilic and lipophilic drugs was examined in this study.

METHODS 5 -Fluoroura cil (5-F U) and clobe tasol 17 -propionat e we re used as the hydrophilic and lipophilic permeants, respectively. In vitro skin delivery using porcine skin and in vivo topical application employing nude mouse as the animal model were both used to examine the effect of microdermabrasion. The vacuum pressures used in this study (15¡V25cmHg) were much lower than those used for therapeutic purposes.

RESULTS The 5 -FU permeation a cross microderma brasion- treate d skin was 8 - to 2 4-fold higher than that across intact skin and depended on differences in treatment pressure and duration. An intensity of 15cmHg for 10 seconds showed the greatest enhancement of 5-FU delivery via the skin. In contrast to the results for 5-FU, microdermabrasion reduced the skin permeation and deposition of topically applied clobetasol. The partitioning effect of clobetasol from the vehicle to the SC may have predominated this result. Microdermabrasion also enhanced the skin delivery of the hydrophilic 5-aminolevulinic acid (ALA). Confocal laser scanning microscopy (CLSM) of microdermabrasion-treated skin revealed intense red fluorescence of ALA-transformed protoporphyrin (PpIX) within the epidermis and upper dermis.

CONCLUSIONS Microdermabra sion can improve the skin permeation of hy drophilic molecules.

The delivery of drugs via the dermal route has been extensively investigated. Nevertheless, clinical applications are limited due to the stratum corneum (SC), the predominant barrier of the skin. This barrier property can be partially overcome by removal of the SC such as with tape stripping. The area and depth of SC treated by tape stripping, however, cannot be precisely controlled. Its safety and the ability of the skin to recover are also questionable. The authors recently suggested that an erbium:YAG laser can effectively enhance and control drug delivery via the skin.1¡V 3 The erbium:YAG laser can ablate the SC with minimal residual thermal damage to the skin. The large size of the device and high price of the laser, however, may limit its applicability. Microdermabrasion is a process that uses Al2O3 crystals and negative pressure to simply peel off the outer surface of the SC.4 Proposed uses for microdermabrasion include the management

of fine rhytides, photoaging, solar lentigines, mild surgical and acne scars, striae, and melasma.5 Microdermabrasion is a simple, rapid procedure that can be repeated easily at short intervals. It is painless, bloodless, noninvasive, and minimally inconvenient for patients.6

Microdermabrasion should improve the permeation of topical medications. The effects of this method on drug delivery, however, have not been systematically investigated. The aim of this study was to evaluate the feasibility of microdermabrasion for enhancing and controlling the topical delivery of drugs. 5-Fluorouracil (5-FU), clobetasol 17-propionate, and 5-aminolevulinic acid (ALA) were used as model permeants in this study because they have already been used clinically through topical application. This present study utilized in vitro Franz cells for determining the transdermal transport of the drugs. Light microscopy, fluorescence microscopy, and confocal laser scanning microscopy (CLSM) were employed to visually characterize the transport pathways and morphology of the skin treated by microdermabrasion.

Materials and Methods

Materials

5-FU, clobetasol 17-propionate, ALA, and fluorescein isothiocyanate (FITC) were purchased from Sigma Chemical Co. (St. Louis, MO). All other chemicals and solvents were of analytical grade.

Microdermabrasion Assembly

The microabrasor (Pepita-C, Mattioli Engineering, Florence, Italy) has a system of aspiration-compression within a flexible tube, which is connected to the machine and a handpiece (4 6 mm). This machine shoots microcrystals of Al2O3 via a nozzle with a variably programmed pressure (15¡V25 cmHg), producing an abrasive effect on the superficial layers of the skin. These microcrystals and the skin debris are aspirated away by another tube connected to the handpiece. The contact duration of the handpiece and skin was 3 to 10 seconds. The application of microdermabrasion was performed by one operator throughout the whole study to avoid the possible difference of the manipulation by different operators.

Histologic Examination by Light Microscopy

Immediately after treatment with microdermabrasion, a specimen of the exposed area of excised pig back skin (Landrace Duroc hybrids, approximately 1 week old) wastakenforhistologicexamination. An adjacent area of untreated skin was assessed as a control. Each specimenwasfixedin10%buffered formaldehyde at pH 7.4 for at least 48 hours. Each section was dehydrated using ethanol, embeddedinparaffinwax,andstained with hematoxylin and eosin. For each sample, three different sites were examined and evaluated under light microscopy (Eclipse 4000, Nikon, Tokyo, Japan).

In Vitro Topical Delivery of Drugs

The diffusion cell used in the in vitro experiment was a Franz vertical diffusion assembly. The porcine skin was mounted with the SC side facing the donor compartment. After treatment with microdermabrasion, the skin surface was wiped with a cotton wool swab several times. The donor compartment (1 mL) contained 5-FU (0.5% w/v) in pH 5 buffer, clobetasol (0.05%) in ethanol pH 7.4 buffer (3:7), or ALA (4%) in pH 5 buffer. The receptor compartment (10 mL) was filled with pH 7.4 citrate phosphate buffer, except the receptor for clobetasol was ethanol pH 7.4 buffer (3:7) for maintaining sink conditions. The available area of the cell was 1.767 cm2. The receptor was maintained at 371C and stirred with a magnetic bar at 600 rpm. At appropriate intervals, 300-mL aliquots of receptor medium were withdrawn and immediately replaced with an equal volume of fresh receptor solution. The drug content in the samples was analyzed by high-performance liquid chromatography methods described previously.2 ,7,8 The amount of 5-FU or clobetasol retained in the skin at the end of the experiment was

also determined based on the method of homogenization.2,9

Fluorescence Microscopy

The in vitro topical application of FITC (250 mM) in pH 7 buffer was performed to examine the FITC distribution within the skin. FITC was applied in the donor compartment for 2 hours. Immediately after treatment, a specimen of exposed area was taken for determination by fluorescence microscopy. The disk-shaped biopsies were cut in half along the diameter, embedded in medium (OCT, Sakura Finetek, Torrance, CA), and frozen in a freezer at ¡V701C. The skin sample wasthensectionedinacryostat microtome. Sections were mounted with glycerin and gelatin. Fluorescence photomicrographs of the sections were obtained with a microscope (Olympus BX-51, Tokyo, Japan) using a filter set having excitation and emission lengths of 470to490and515to700nm, respectively.

CLSM

The protoporphyrin (PpIX) distribution within the skin after in vivo topical application of ALA was examined by CLSM. A glass cylinder with an available area of 0.785 cm2 was placed on the back skin of a female nude mouse (Balb/c-nu strain, 8 weeks old) with glue. ALA pH 5 buffer (0.2 mL) at a concentration of 4% was added to each cylinder. The vehicles were applied to the skin either with or without microdermabrasion treatment. The application duration was 2 hours. After excising the skin, the full skin thickness was optically scanned at 7- to 10-mm increments through the Z-axis of a confocal microscope (TCS SP2, Leica Microsystems GmbH, Wetzlar, Germany). Optical excitation was carried out with a 488-nm argon laser beam, and the fluorescence emission was detected at 590 nm.

Statistical Analysis

The statistical analysis of differences between different treatments was performed using an unpaired Student¡¦s t-test. A level of probability of .05 was taken as the level of significance.

Results

Histologic Examination of Porcine Skin

Porcine skin was treated with microdermabrasion for 3, 5, and 10 seconds at 15 cmHg to assess the effect of microdermabrasion on the integrity of the skin structure. The vacuum suction powers tested in this study were lower than those utilized for therapeutic purposes.4, 10,11 Light microscopy indicated no observable damage to the whole skin in the nontreated sample as shown in Figure 1A. Microscopic evaluation of skin sections showed no gross changes in the structural features of the skin with 3- and 5-second treatments (data not shown). Light microscopy showed a slight thinning of the SC after a 10-second treatment at 15 cmHg (Figure 1B). The SC was homogenized and focally compacted. Retention of Al2O3 crystals was not observed on the surface of the SC. No changes in the viable epidermis or dermis of skin treated for 10 seconds were noted when compared to the control.

The skin was exposed to a higher pressure of 25 cmHg for 5 seconds. The morphologic changes of the treated skin were more significant than those with 15 cmHg for the same treatment duration (data not shown). A similar observation was made between the intensity of 15 cmHg for 10 seconds and 25 cmHg for 5 seconds. A higher focal compaction of the SC was seen with 25cmHg for 5 seconds because there were almost no voids between the SC and epidermal layers.

Topical Application of 5-FU and Clobetasol by Microdermabrasion

5-FU and clobetasol were chosen as the hydrophilic and lipophilic permeants, respectively. Figure 2 depicts the influence of microdermabrasion on the skin permeation of 5-FU, and the cumulative amount of 5-FU (mg/cm2) in the receptor compartment as a function of application time is shown. The permeation data of various formulations were analyzed using the following equation based on the Fick¡¦s law:

$$Js\ s \quad dQ=edt\ AT;$$

where Js s is the flux at steady state, Q is the cumulative mass of drug transferred to the receptor

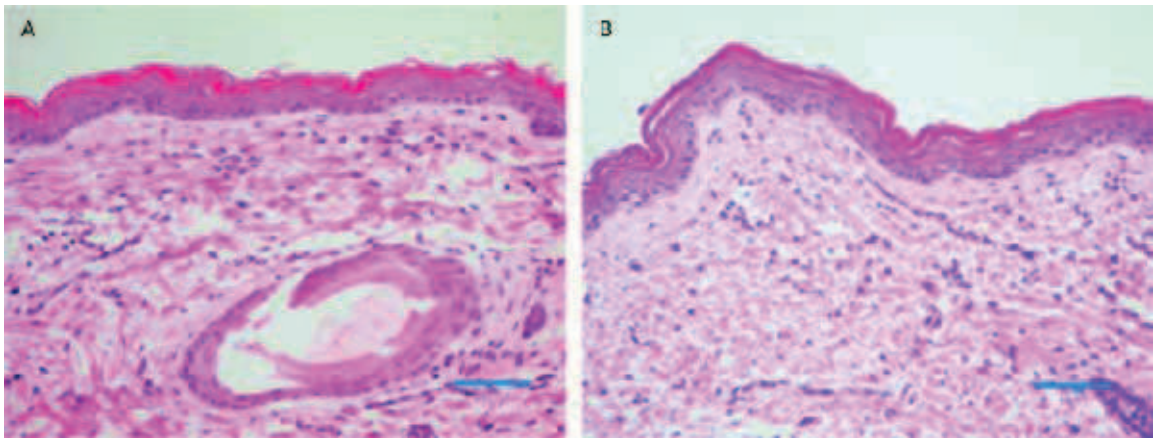

Figure 1. Histologic examination of porcine back skin with (A) no treatment and (B) microdermabrasion for 10 seconds at 15 cmHg (original magnification, 200). Porcine skin was treated with or without microdermabrasion. Immediately after treatment, the skin species were fixed in buffered formaldehyde at pH 7.4 for 48 hours. Each section was dehydrated and stained by hematoxylin and eosin. The appearance of skin was examined under light microscopy. The observation is demonstrated as follows: (A) An intact and typical porcine skin structure is seen. No observable damage to the whole skin; (B) a slight thinning of the SC is demonstrated. The SC layers appear to be concentrated and focally compacted. No change is seen in the layers of epidermis and dermis.

phase, and A is the diffusion area of the skin. The slopes of the resulting plots were computed, and the slopes from 0 to 12 hours of the application duration were calculated as flux (mg/cm2/hr) (Table 1). 5-FU exhibited very low permeation in the control without microdermabrasion treatment. Figure 2 demonstrates that microdermabrasion was effective in enhancing skin permeation to 5-FU for all intensities used (po.05). The treatment durations of 3, 5, and 10 seconds at 15 cmHg, respectively, produced 5.23-, 4.35-, and 11.06-fold increases in 5-FU delivery compared to the control. The effect of vacuum pressure on the permeation of 5-FU was also examined. A higher pressure (25 cmHg for 5 seconds) only reached a similar enhancement compared to the lower pressure (15 cmHg for 5 seconds; p4.05).

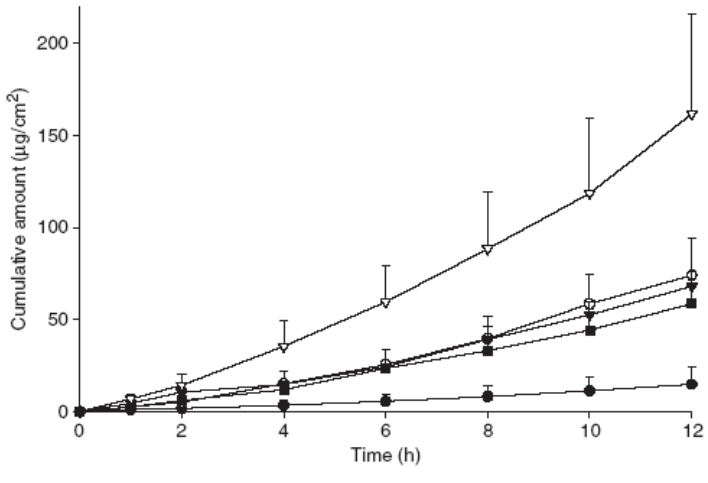

Figure 2. In vitro cumulative amount-time profiles of topical 5-FU permeation with microdermabrasion treatment of skin at various intensities: ( ) control group; (J) 15cmHg for 3 seconds; (.) 15 cmHg for 5 seconds; (,) 15 cmHg for 10 seconds; and (&) 25cmHg for 5 seconds. Each value represents the mean 7 standard deviation (n = 4).

Figure 3 shows the cumulative amount¡Vtime profiles of clobetasol delivery via microdermabrasion-treated skin. In contrast to the results for 5-FU, clobetasol delivery across treated skin was dramatically lower (po.05) than that across intact skin. The clobetasol flux after microdermabrasion treatment with 3, 5, and 10 seconds only reached the flux without treatment by percentages of 8, 13, and 23%, respectively.

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TABLE 1. The Flux and Skin Deposition of 5-FU across Pig Skin Pretreated by Microdermabrasion*

Pressure (cmHg)	*Duration (sec)*	*Flux (µg/cm2/hr)*	*Skin Deposition (µg/mg)*
0	0	1.19 ± 0.82	0.14 ± 0.04
15	3	6.22 ± 1.68†	0.11 ± 0.03
15	5	5.18 ± 1.11†	0.10 ± 0.04
15	10	13.16 ± 4.23†	0.13 ± 0.06
25	5	4.83 ± 1.48†	0.06 ± 0.01‡

*Each value represents the mean ± standard deviation ($n = 4$). †$p < .05$ higher compared to the control. ‡$p < .05$ lower compared to the control.

The clobetasol flux decreased after a decrease in the application duration at 15 cmHg (Table 2). The intensity of 25 cmHg for 5 seconds produced higher clobetasol permeation (po.05) than treatment at 15 cmHg. The skin deposition of clobetasol was determined at the end of the in vitro experiment (12 hours). As shown in Table 2, there was a smaller clobetasol depot (po.05) after treatment compared to the nontreated group.

Fluorescence Microscopic Observations

Because microdermabrasion may be feasible for enhancing the skin delivery of hydrophilic molecules, the mechanisms for this enhancement were studied by examining the fluorescence microscopic appearance. FITC was used as a model for hydrophilic molecules to determine the fluorescence signal within the skin. Figure 4A shows a microscopic photomicrograph from a nontreated (control) site of skin with FITC permeation for 2 hours. The fluorescence signal was mainly detected in the SC with no evidence of the delivery of FITC into the viable epidermis/dermis. FITC was also primarily localized in the hair follicles, suggesting that appendageal routes may be important for FITC delivery. For the site exposed to a microdermabrasion intensity of 15 cmHg for 10 seconds as shown in Figure 4B, there was a broad and continuous band of a fluorescence signal that extended from the SC into deeper layers of the epidermis. The fluorescence intensity of the skin treated with 25 cmHg for 5 seconds was less than that of skin treated with 15 cmHg for 10 seconds (data not shown).

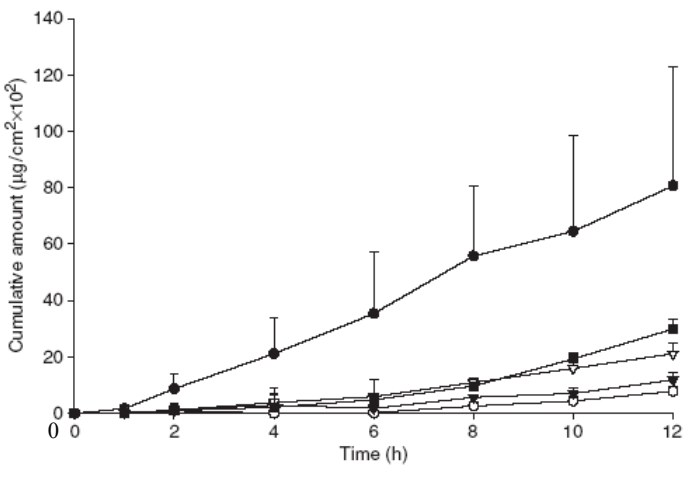

Figure 3. In vitro cumulative amount¡Vtime profiles of topical clobetasol permeation with microdermabrasion treatment of porcine skin at various intensities: ( ) control group; (J) 15 cmHg for 3 seconds; (.) 15 cmHg for 5 seconds; (,) 15 cmHg for 10 seconds; and (&) 25 cmHg for 5 seconds. Each value represents the mean 7 standard deviation (n = 4).

Topical Application of ALA by Microdermabrasion

Table 3 shows the ALA flux across porcine skin after in vitro topical delivery. ALA possessed very low permeation in the group without microdermabrasion. The disruption of the SC by microdermabrasion reduced the inherent barrier properties of the skin to ALA and thus enhanced permeation across the skin (Table 3). A 39-fold increase in the ALA flux was observed with an intensity of 15 cmHg for 10 seconds. The enhancement of ALA permeation by 25 cmHg for 5 seconds was lower than that by 15 cmHg for 10 seconds, although there was no statistically significant difference (p4.05) between them. Because nude mouse was to be used as the

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TABLE 2. The Flux and Skin Deposition of Clobetasol across Pig Skin Pretreated by Microdermabrasion*

Pressure (cmHg)	*Duration (sec)*	*Flux ($\mu g/cm^2/hr \cdot 10^2$)*	*Skin Deposition ($\mu g/mg \cdot 10^2$)*
0	0	6.99 ± 3.57	2.54 ± 0.39
15	3	$0.56 \pm 0.15^{\dagger}$	$1.16 \pm 0.30^{\dagger}$
15	5	$0.94 \pm 0.30^{\dagger}$	$1.44 \pm 0.25^{\dagger}$
15	10	$1.64 \pm 0.18^{\dagger}$	$1.43 \pm 0.40^{\dagger}$
25	5	$2.33 \pm 0.26^{\dagger}$	$1.66 \pm 0.39^{\dagger}$

*Each value represents the mean $\pm$ standard deviation ($n=4$). $^{\dagger}p<.05$ lower compared to the control.

animal model for in vivo ALA application, the in vitro permeation experiment using nude mouse skin as a barrier was also performed. It was expected that nude mouse skin would be more permeable than porcine skin as shown in Table 3. Microdermabrasion with an intensity of 15 cmHg for 10 seconds showed a more efficient increase in ALA permeation across nude mouse skin than across pig skin (48-fold vs. 39-fold). The enhancement by 25 cmHg for 5 seconds was much lower (po0.05) than that by 15 cmHg for 10 seconds. This result somewhat differed from the result for porcine skin.

CLSM Observations

Figure 5 shows confocal images obtained from control and microdermabrasion-treated samples of nude mouse skin after in vivo ALA administration for 2 hours. The full skin thickness was optically scanned at 7- to 10-mm increments for 16 fragments from the surface of the skin (left to right, top to bottom). Compared to the control (Figure 5A), increased red fluorescence of PpIX in the skin after treatment could clearly be seen with intense signals (Figure 5B). The fluorescence signal with 15 cmHg for 10 seconds was greater than that with 25 cmHg for 5 seconds. For the site exposed to microdermabrasion, there was a broad distribution of red fluorescence that extended from the epidermis into the upper dermis. The fluorescence gradient in the treated skin decreased with tissue thickness from the epidermis to the dermis.

Discussion

Microscopic examination of the skin showed that no Al2O3 crystals remained on the surface of the SC after the procedure. The concern about the Al2O3 hazard to skin can be avoided after microdermabrasion treatment.1 2 Histo-

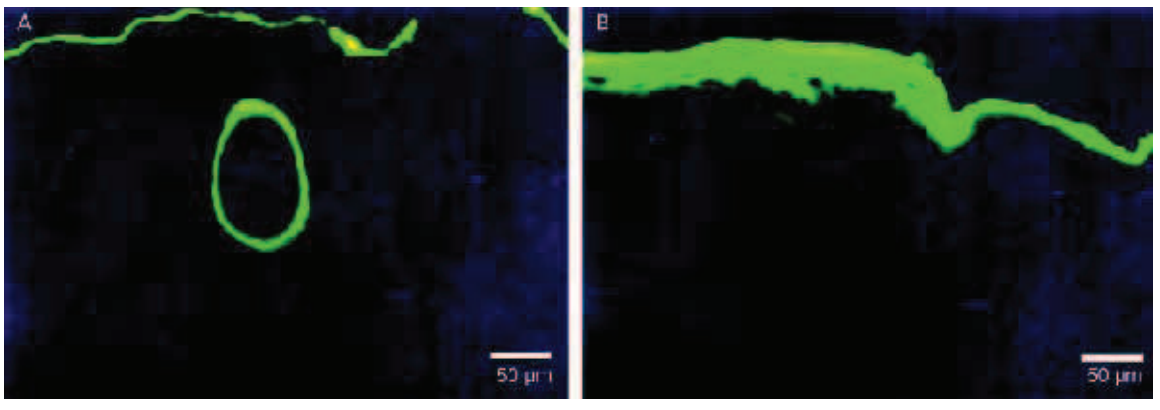


Figure 4. Fluorescence microscopic examination after topical administration of FITC via porcine back skin for 2 hours: (A) nontreated skin and (B) microdermabrasion treatment with 15 cmHg for 10 seconds (original magnification, 200). FITC with a dose of 250 mM was administered to the porcine skin in vitro. The applied duration was 2 hours. Immediately after treatment, the specimen of exposed area was cut in half along the diameter and embedded in OCT. The section was mounted with glycerin and gelatin. The appearance of skin was examined under fluorescence microscopy. The observation is demonstrated as follows: (A) The fluorescence signal is mainly detected in the skin surface with no evidence in the epidermis and dermis. The signal is significant in a hair follicle. (B) There is a broad and continuous band of a fluorescence signal that extended from the SC into deeper layers of the epidermis.

TABLE 3. The Flux (μg/cm²/hr) of ALA across Pig Skin and Nude Mouse Skin Pretreated by Microdermabrasion*

Pressure (cmHg)	*Duration (sec)*	*Pig Skin*	*Nude Mouse Skin*
0	0	1.96 ± 0.25	5.66 ± 2.01
15	10	76.19 ± 16.94†	274.04 ± 35.09†
25	5	56.87 ± 10.21†	98.27 ± 28.67†

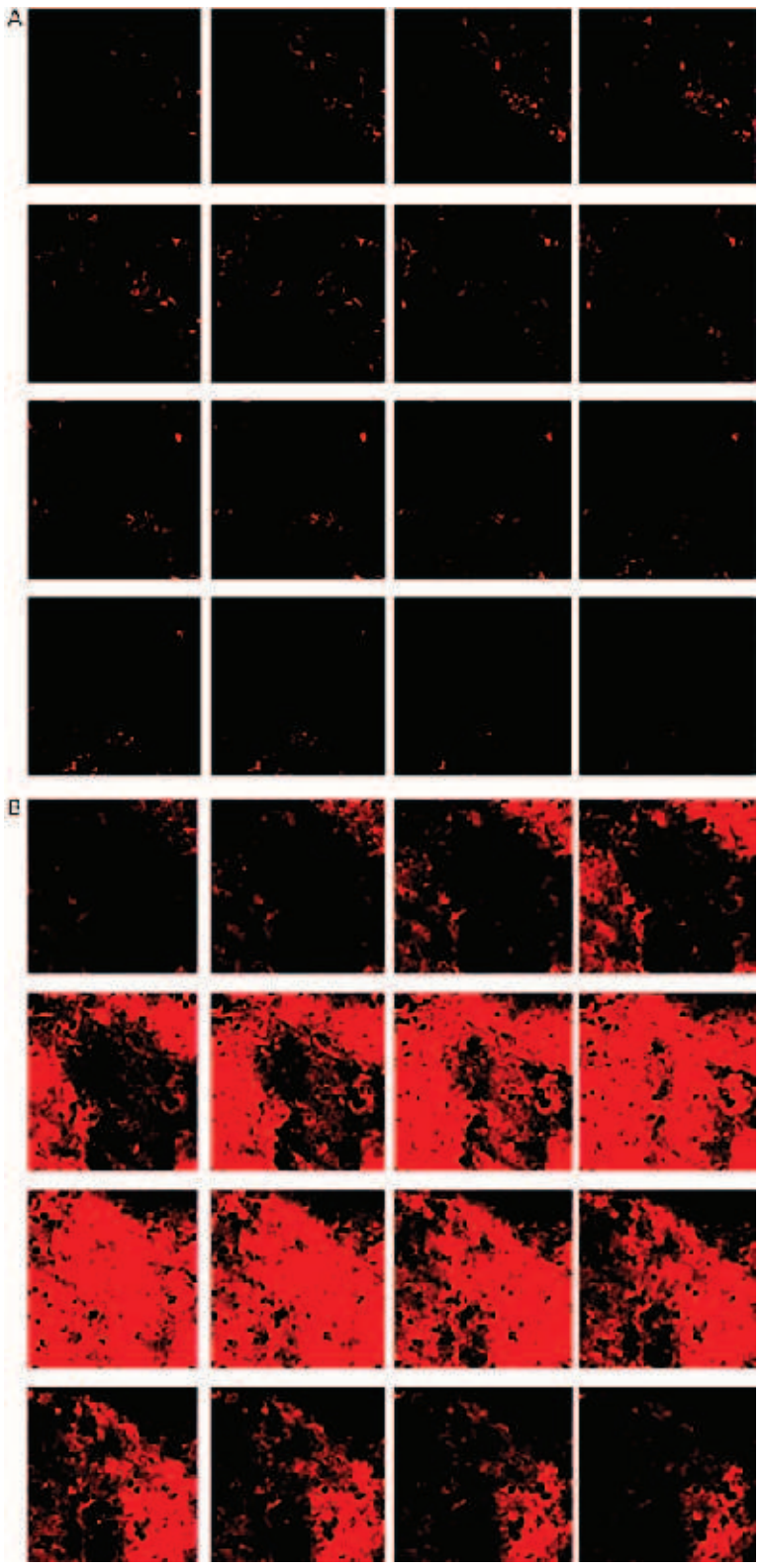
*Each value represents the mean ± standard deviation ($n = 4$). †$p < .05$ higher compared to the control.

with microdermabrasion indicated that it may simply remove and compact the SC layers while preserving the intact epidermis/dermis. The mechanism by which microdermabrasion produces abraded skin is based on high-speed compressed Al2O3 crystals. The depth of peeling is controlled by the programmed pressure. This can theoretically prevent deep-tissue damage and allow precise control of ablation of the skin. A previous study also showed that the degree of damage is less severe after physical microdermabrasion compared with chemical glycolic acid peeling in a clinical situation.1 3

5-FU is a hydrophilic and negatively charged molecule, which is difficult to transport across intact skin.14 As can be seen in Figure 2, 5-FU showed an inherent low permeation across the skin without treatment. This may indicate that the SC has a more pronounced barrier effect on more hydrophilic molecules. Although no gross changes in the SC structure were observed by subjective observations with microscopy, 3- and 5-second treatments of microdermabrasion at 15 cmHg were sufficient to enhance 5-FU flux by 4- to 5-fold. The treatment duration of 10 seconds showed higher enhancement than those of shorter durations at the same pressure. This study showed that microdermabrasion pretreatment limited the area of drug diffusion area by 42.67% (0.754-cm2 oval-shaped handpiece/1.767-cm2 diffusion area) of the total permeated skin surface. Extrapolating the original flux of the treated area to an area of 100% exposure resulted in an enhancement ratio of 24.57 with 15 cmHg for 10 seconds. According to the standard deviation shown in the permeation data of 5-FU (Table 1), the intersubject variation was not large after microdermabrasion treatment. This is a good result because porcine skin usually shows large discrepancies among subjects. The same phenomenon is also observed in humans. Unlike many dermabrasion techniques in which skin ablation is quite operator-dependent, microdermabrasion penetration is predominantly based on the programmed setting.5,12 This may provide a distinct advantage over tape stripping, which is both macroscopic and, to some extent, unpredictable.15

Factors that may affect drug permeation include the size of the molecule, its affinity to the surface of the skin, and its compatibility with the intercellular lipids.16 Because the SC is a lipophilic barrier in the skin, the lipophilic clobetasol easily partitions into the SC, after which it passes across the skin. Previous studies also indicated that the SC/vehicle partition coefficient plays an important role in the amount of corticosteroids such as clobetasol and betamethasone released from the vehicle to the skin.17,18 The ablation and homogenization of the SC layers may reduce the inherent barrier properties of the SC and thus increase the skin delivery of drugs; however, the partitioning of lipophilic permeants into the SC may be reduced because of the limited area of the SC after microdermabrasion exposure.3 As a result, the increased permeation of the skin due to ablation may be partly offset by a reduction in partitioning. A previous report also showed a dramatic decrease in the skin surface sebum immediately after microdermabrasion treatment.6 This may further provide an unfavorable environment for clobetasol delivery into the skin.

The molecular weights of 5-FU, clobetasol, and ALA are 130, 467, and 168 Da, respectively. Microdermabrasion was beneficial to both molecules with smaller sizes (5-FU and ALA). This indicates that the permeation enhancement by microdermabrasion may prefer to the drugs with low molecular size in



the conditions used in this study. The authors may not expand this trend beyond this study, however, because the molecular weight range of different drug models used in this study is narrow. Further study is needed and in progress to explore the real mechanisms.

There was lower clobetasol deposition (po.05) within the skin after treatment compared to the nontreated group. This suggests that microdermabrasion may partly ablate the SC, resulting in a reduction in clobetasol partitioning into the skin reservoir. The skin deposition of 5-FU was also examined as shown in Table 1. No significant differences (p4.05) were observed between the skin

Figure 5. Confocal laser scanning microscopic (CLSM) micrographs of nude mouse skin after in vivo topical administration of ALA via nude mouse skin for 2 hours: (A) nontreated skin and (B) microdermabrasion treatment with 15 cmHg for 10 seconds (original magnification, 20). ALA with a dose of 4% (w/v) was administered to the back skin of nude mouse in vivo. The applied duration was 2 hours. After excising the skin, the specimen was viewed by CSLM at 7- to 10-mm increments through the Z-axis. The full thickness was divided to 16 fragments from the surface of the skin (left to right, top to bottom). The observation is demonstrated as follows: (A) A weak intensity of fluorescence is represented. Some fluorescence spots appeared within the skin. ALA penetrates the mouse skin to 120 to 130 mm from the skin surface. (B) There is a broad distribution of red fluorescence throughout the whole skin. The fluorescence intensity gradually increases from the skin surface and reaches the maximal level at the depth of 70 to 100 mm. Then the fluorescence signal decreases following the increase of skin depth till skin bottom.

deposition of 15 cmHg¡Vtreated groups and the control. Although the removal of the SC barrier greatly enhances 5-FU permeation, improvement of drug partitioning into the SC layers is still important for 5-FU delivery via the skin.2,14, 19 Another explanation may be the saturation of 5-FU in the skin reservoir, which hinders the further increment in 5-FU deposition. A treatment intensity of 25 cmHg for 5 seconds produced lower skin deposition compared to the other intensities (po.05; Table 1). This may have been due to the more condensed SC layers treated by 25 cmHg for 5 seconds leading to limited space in which 5-FU could be partitioned. This may have confined the subsequent 5-FU permeation across the skin to a certain level (Figure 1).

In the fluorescence microscopic observations of hydrophilic FITC in the skin, a broad and continuous band of fluorescence signal was detected with the 15 cmHg for the 10-second exposure. This result indicates that microdermabrasion increases the transport of hydrophilic permeants via both transcellular and intercellular regions. The 25 cmHg treatment for 5 seconds produced a thinner band of fluorescence compared to the 15 cmHg treatment for 10 seconds. The more condensed SC structure may have produced limited space for the distribution of topically administered FITC. This result is in accordance with the lower deposition of 5-FU within the skin treated with 25 cmHg for 5 seconds.

ALA is used as a precursor of PpIX for photodynamic therapy of superficial skin cancers and subcutaneous metastases of internal malignancies. The permeability of hydrophilic ALA across intact skin is always low, making it difficult to achieve the desired therapeutic benefits.20,21 As expected, microdermabrasion was useful for improving the topical delivery of ALA via porcine skin because the rate-limiting step for ALA uptake into the skin lies at the level of the SC.

The result of CLSM after in vivo topical ALA delivery showed that the fluorescence signal with treatment at 15 cmHg for 10 seconds was greater than that with 25 cmHg for 5 seconds. This profile is consistent with the in vitro ALA flux. The higher ALA deposition within the skin may promote subsequent ALA delivery from the skin to the subcutaneous regions. A previous study revealed that immediately after the procedure of microdermabrasion, thermal photography showed increased skin temperature, consistent with increased blood flow.6

Both skin disruption and increased blood flow contribute to the in vivo increment of ALA delivery via nude mouse skin. Microdermabrasion may exhibit more prominent enhancement of drug delivery in an in vivo status. This explanation, however, needs to be further explored because the pressure used in this study was lower than that used clinically. Of course the more complex condition in the in vivo status may increase the difficulty of the microdermabrasion application. The positive results shown in this study, however, have encouraged the future in vivo investigation about the enhancing efficiency of microdermabrasion on drug delivery via skin. A significant distribution of red fluorescence extended from the epidermis to the upper dermis. This may have been due to epidermal cells synthesizing a much higher quantity of porphyrins than fibroblasts. Also, ALA-induced porphyrins are preferentially localized in the epithelial lining of the skin.2 2

Conclusions

Microdermabrasion used in this study has been suggested as a good method for enhanced and controlled drug delivery via the skin. Microdermabrasion increases the skin permeation of hydrophilic drugs simply by partially ablating and homogenizing the SC layers. Both SC barrier reduction and drug partitioning into the skin may contribute to the mechanisms affecting 5-FU permeation across treated skin. It was suggested that the effect of skin barrier reduction was superior to the partitioning of 5-FU in the skin for enhancing 5-FU delivery. Modulation of the application duration may further increase 5-FU permeation instead of modulation of vacuum

pressure. In the case of clobetasol, partitioning may play an important role governing skin permeation; thus a negative effect on skin delivery was seen after treatment. The microdermabrasion procedure examined in this study enhanced ALA permeation by 40- to 50-fold, and this might reduce the ALA dose required, so the cost of photodynamic therapy may also be reduced. It should be careful to adjust the ALA dose after microdermabrasion treatment, however, because the greater amount of ALA in skin leads to the risk of intense erythema associated with photodynamic therapy. This study has demonstrated that microdermabrasion is an effective alternative treatment for enhancing and controlling the delivery of hydrophilic molecules via skin routes. It is also safe and simple to apply.

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