



Optimization of microdermabrasion for controlled removal of stratum corneum

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ARTICLE INFO

Article history:

Received 8 September 2010

Received in revised form

13 December 2010

Accepted 17 January 2011

Available online 25 January 2011

Keywords:

Microdermabrasion

Skin

Stratum corneum

Transdermal drug delivery

ABSTRACT

Microdermabrasion has been shown to increase skin permeability for transdermal drug delivery by damaging or removing skin's outer layer, stratum corneum. However, relationships between microdermabrasion parameters and effects on the stratum corneum barrier have not been developed. In this study, we determined the effect of microdermabrasion crystal flow rate, time, and suction pressure applied in both static and dynamic modes on the extent of stratum corneum removal from excised porcine skin. In addition to controlling the depth of tissue removal by microdermabrasion parameters, we also controlled the area of tissue removal by applying a metal mask patterned with 125- or 250- μm holes to selectively expose small spots of tissue to microdermabrasion. We found that the extent of stratum corneum removal depended strongly on the crystal flow rate and exposure time and only weakly on pressure or static/dynamic mode operation. Masking the skin was effective to localize stratum corneum removal to exposed sites. Overall, this study demonstrates that optimized microdermabrasion in combination with a mask can be used to selectively remove stratum corneum with three-dimensional control, which is important to translating this technique into a novel method of transdermal drug delivery.

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1. Introduction

Transdermal drug delivery involves the administration of drugs, usually from transdermal patches or topical formulations, across the skin's surface and typically into the systemic circulation (Prausnitz and Langer, 2008; Williams, 2003). This is a convenient and desirable route of delivery because skin offers a large area for delivery, therapeutics can be administered in a consistent dose that avoids the first pass effect of the liver, and needle-free delivery avoids pain and the dangers associated with hypodermic injection. Despite the ease of drug delivery using transdermal patches and ointments, the anatomy of skin only allows small amounts of low molecular weight, lipophilic molecules, such as estrogen and nicotine, to penetrate intact skin at therapeutic levels. This is because the main barrier to transdermal transport is the stratum corneum, which is the outer 10–15 μm layer of skin. The stratum corneum is composed of nonviable corneocytes that are surrounded by a lipid extracellular matrix. The viable epidermal and dermal layers beneath the stratum corneum typically offer much less resistance to drug transport.

To overcome the stratum corneum barrier and increase skin's permeability to hydrophilic and macromolecular compounds, the stratum corneum is often pierced for injection or removed by stripping, ablation, or abrasion (Arora et al., 2008; Banga, 2009). Devices that pierce the stratum corneum involve the use of hypodermic needles, microneedles, or jet injectors (Baxter and Mitragotri, 2006; Prausnitz et al., 2009). These methods lend themselves to bolus delivery and are typically either invasive, painful or both. Stratum corneum removal can be done by tape stripping, but the procedure is time consuming and requires expert technique (Fujimoto et al., 2005). Ablation utilizes energy generated by lasers or heating elements to remove the stratum corneum (Banga, 2009). Abrasion uses sandpaper or pressurized particles, such as microdermabrasion, to remove the stratum corneum (Fang et al., 2004; Fujimoto et al., 2005; Gill et al., 2009; Lee et al., 2003, 2006; Song et al., 2004). The advantage to using abrasion is that it is quick and painless, and that microdermabrasion is already approved by the FDA for other applications. However, current microdermabrasion equipment requires detailed characterization to determine conditions that selectively remove stratum corneum for transdermal drug delivery. Because it is the rate-limiting barrier, removal of stratum corneum by microdermabrasion can dramatically increase skin permeability, even to large molecules including proteins and vaccines (Gill et al., 2009).

Microdermabrasion is an FDA-approved cosmetic procedure that was developed in the 1980s to reduce the appearance of large pores, fine lines, wrinkles, tattoos, and superficial scars (Bhalla and Thami, 2006). Microdermabrasion damages the stratum corneum

Abbreviations: H&E, hematoxylin and eosin.

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by bombarding it with abrasive particles, such as alumina or sodium chloride, under vacuum (Rajan and Grimes, 2002). Damaging stratum corneum induces an inflammatory response that results in increased collagen remodeling and proliferation, which produces the positive cosmetic results seen after microdermabrasion treatment, such as noticeably firmer skin (Freedman et al., 2001).

The microdermabrasion machine works by placing a handpiece on the skin, which occludes the opening of the plastic tip to create a vacuum. Upon tip occlusion, the crystals flow from the machine into the inlet port and abrade the skin. At the same time, the skin debris and used crystals are shunted back through the outlet port to the machine and collected in a waste container. This closed-loop system prevents cross-contamination between patients and exposure of medical personnel. Typically, patients undergo several sessions of microdermabrasion, depending on the severity of the skin condition, to improve the skin's appearance (Freedman et al., 2001; Shim et al., 2001). The procedure is noninvasive, painless, and short, and requires no down time for recovery. Typically, microdermabrasion is performed at spas or by cosmetic surgeons or dermatologists.

Several studies have shown that microdermabrasion can be used to increase transdermal delivery of low molecular weight compounds such as vitamin C (176 Da), 5-aminolaevulinic acid (130 Da), 5-fluorouracil (467 Da), lidocaine (234 Da) and estradiol (272 Da) (Fang et al., 2004; Fujimoto et al., 2005; Herndon et al., 2004; Lee et al., 2003; Lee et al., 2006). We also showed in a previous study that microdermabrasion can be used to completely remove the stratum corneum in humans and monkeys and demonstrated increased skin permeability to fluorescein (332 Da) and a model viral vaccine (Modified Vaccina Ankara) (Gill et al., 2009). Abrasion can also be used in conjunction with a mask to minimize and control the area of abrasion (Herndon et al., 2004).

Building off these previous findings, this study sought to develop a microdermabrasion method that offers three-dimensional control over stratum corneum removal, which should provide improved control over transdermal drug delivery. Control over depth of abrasion, and the ability to completely remove stratum corneum without damaging deeper tissue, was pursued through a detailed analysis of the effects of microdermabrasion crystal flow rate, time, suction pressure, and handpiece movement. To control the area of abrasion, we designed a mask to cover the skin and allow microdermabrasion to occur only through small holes in the mask, thereby localizing tissue removal to specific locations. In this way, we could control the size of holes made in the skin by microdermabrasion in all three dimensions.

2. Materials and methods

2.1. Microdermabrasion procedure

Microdermabrasion experiments were conducted on excised adult feeder porcine (2–9 month old, average weight 32 kg) dorsal skin (Pel-freeze Biologicals, Rogers, AR) using a Gold Series MegaPeel microdermabrasion machine (DermaMed USA, Lenni, PA) with the gold handpiece assembly. Pig skin was obtained with approval from the Georgia Tech Institutional Animal Care and Use Committee. The skin was stored at -70°C prior to use. Before the experiments were conducted, subcutaneous fat was removed from the skin using a scalpel (Fisher Scientific, Fair Lawn, NJ) and the hair was carefully removed using surgical prep razors (Medex Supply, Monsey, NY) without damaging the skin.

A picture of a microdermabrasion machine tip and the alumina crystals are shown in Fig. 1A and B, respectively. The experiments were carried out using two different abrasion modes: static and dynamic. For the static mode, the machine handpiece remained stationary on the skin for 6 s. For the dynamic mode, it was moved

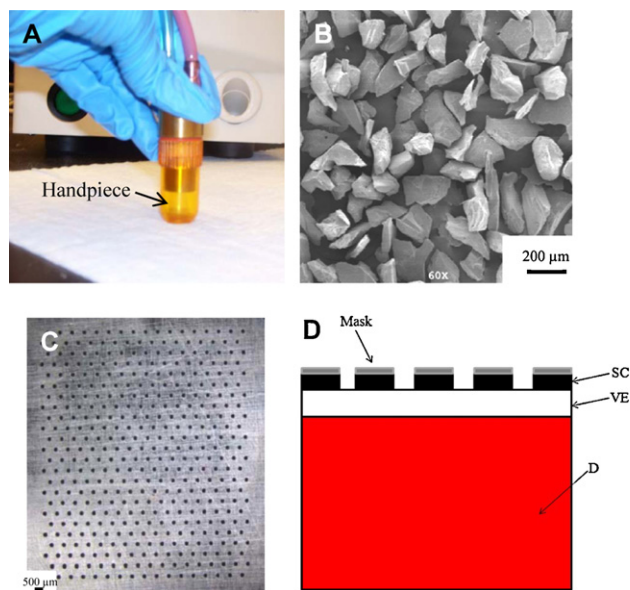


Fig. 1. Microdermabrasion device and mask. (A) Microdermabrasion machine handpiece and (B) the alumina abrasion crystals ($\sim 100\ \mu\text{m}$ in diameter). (C) Stainless steel mask with 408 holes ($125\ \mu\text{m}$ diameter). (D) Schematic diagram of the skin after abrasion with the mask, where the stratum corneum is selectively removed and the underlying layers are intact. SC = stratum corneum, VE = viable epidermis, and D = dermis.

along the skin for 10 passes at a rate of 1 pass/s. The dynamic mode experiments were carried out by first isolating the area of abrasion with a rectangular foam adhesive (Avery Dennison, Painesville, OH) having inner dimensions measuring 41 mm long and 15 mm wide and sliding the probe back and forth within this area.

For both abrasion modes, the effect of crystal flow rate and suction pressure was examined. The crystal flow rate was varied from the minimum value (corresponding to a setting of 9 turns of the crystal flow rate knob on the microdermabrasion machine) to the maximum value (corresponding to a setting of 0 turns of the crystal flow rate knob). As discussed in Appendix A, we determined this range of crystal flow rates to span 8.9×10^2 – 2.2×10^5 particles/s or <0.01 – 0.80 g/s of particles. The suction pressure was also varied from -30 kPa to -60 kPa. All experiments were carried out in triplicate.

We also studied the effect of time on depth of skin abrasion as a function of the crystal flow rate and pressure for the static and dynamic abrasion modes using porcine skin. For the static mode, the crystal flow rate was fixed at 4 turns and the time points studied were 3, 20, and 45 s at suction pressures of -30 , -40 , and -50 kPa. For the dynamic mode, the flow rate was set to 4.5 turns and the suction pressures examined were -25 and -45 kPa for 1, 10, and 50 passes. All experiments were carried out in triplicate.

At the conclusion of each experiment, an 8 mm skin biopsy was taken with a biopsy punch (Miltex Inc, York, PA), embedded in optimal cutting temperature compound (Sakura Finetek, Torrance, CA) and frozen in dry ice for histological analysis. The skin was sectioned using a Leica 3050S cryostat (Leica Microsystems, Wetzlar, Germany) at a thickness of $10\ \mu\text{m}$, stained with routine hematoxylin and eosin (H&E), and imaged using a Nikon 600E microscope (Nikon, Tokyo, Japan) and Qcapture software (Q Imaging, Pleasanton, CA).

2.2. Abrasion depth quantification

The depth of abrasion was quantified by assigning values to indicate the degree of stratum corneum removal. For the experiments in which the time was held constant, 0 indicated stratum corneum

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